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CONTENTS

PAGE

The Familial Incidence of Congenital Malformation of the Heart. By THOMAS MCKEOWN, BRIAN MACMAHON, AND C. G. PARSONS 273

Ballistocardiograms after Cigarette Smoking in Health and in Coronary Heart Disease. By C. B. HENDERSON 278

Congenital Tricuspid Atresia. By ROY ASTLEY, J. S. OLDHAM, AND CLIFFORD PARSONS 287

Left Atrial and Pulmonary Capillary Venous Pressures in Mitral Stenosis. By R. G. EPPS AND RICHARD ADLER 298

Persistent Left Superior Vena Cava Draining the Pulmonary Veins. By FRANCES GARDNER AND SAMUEL ORAM 305

The Angiocardiogram in Fallot's Tetralogy. By JAMES B. LOWE 319

Fatality following Cardiac Catheterization Injury. By J. F. GOODWIN 330

Necropsies in some Congenital Diseases of the Heart, mainly Fallot's Tetralogy. By W. D. BRINTON AND MAURICE CAMPBELL 335

Cation Exchange Resin (Resodec) in the treatment of Cardiac Œdema. By A. A. FITZGERALD PEEL AND T. SEMPLE 350

CASE REPORTS

A-V Dissociation in Dystrophia Myotonica. By J. A. LITCHFIELD 357

Ebstein's Anomaly Diagnosed during Life. By C. B. HENDERSON, FREDERIC JACKSON, AND W. G. A. SWAN 360

Abstracts of Cardiology 364

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THE FAMILIAL INCIDENCE OF CONGENITAL MALFORMATION OF THE HEART

BY

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Received October 23, 1952

It is generally believed that the incidence of congenital malformation of the heart is raised in relatives of affected individuals. The evidence in support of this view consists mainly of isolated records of families with more than one affected member (Courter *et al.*, 1948, refer to 63 reported cases), but a few examples have been noted in the course of investigations of large series of patients (for example, by Abbott, 1927; Dogramaci and Green, 1947; Campbell, 1949; and Lamy and Schweisguth, 1950, among others). Such observations are suggestive, but scarcely justify a confident assertion that incidence in relatives is raised, since both the numbers of relatives at risk and the incidence of affected in the related general populations were unknown. In the present communication we give the numbers of affected and unaffected relatives of a series of patients with various congenital cardiac malformations. All known affected relatives were recorded during the enquiry, but observations on incidence are restricted to brothers, sisters, parents, and first cousins of propositi. The data suggest that incidence of congenital malformation of the heart is raised in sibs, but is not raised in parents and cousins of affected individuals.

Material. We have previously described an investigation in which an attempt was made to record all cases of congenital malformation of the heart in children born to Birmingham mothers in the years 1940–49 (MacMahon *et al.*, 1953): 633 affected were identified in a population of 194,418 births, but for investigation of familial incidence we have used only 478 in which the diagnosis was confirmed post mortem (236), at operation (19), or clinically by a consultant physician (223); many of the cases were also investigated thoroughly. Of the 478 propositi, 431 (90%) drawn from 425 fraternities, were traced by field enquiry and family histories recorded. Where a history of congenital heart disease in a relative was elicited, the diagnosis was checked if possible by reference to hospital records or by examination by one of us (C.G.P.).

While accepting the diagnosis of congenital heart disease in all 431 propositi traced, we have accepted the diagnosis of the specific cardiac defect only in cases examined post mortem (206) or at operation (17).

INCIDENCE IN SIBS

In the 425 fraternities for which data are available there were 1012 sibs of the first propositus in each fraternity (that is of the first affected individual born in Birmingham in the period 1940–49); of these 646 were born before, 352 were born after, and 14 were twins of propositi. The incidence of malformations in sibs born before is of little interest, and we confine attention to the 352 sibs born after first propositi. They are derived from fraternities of two kinds: (*a*) 417 in which the

* In receipt of a grant from the Medical Research Council.

first malformed individual was a propositus; and (*b*) 8 in which the first malformed individual was not a propositus, being born before 1940. Fraternities under (*b*) are unrepresentative, since they come to attention only because a second malformation has occurred. It follows that if the likelihood of a third malformation in a fraternity is greater than of a second, the incidence in later sibs will be too high if they are included. We therefore restrict examination of incidence to the 417 fraternities under (*a*).

Table I shows that there were 6 affected among the 342 sibs born after the first propositus in 417 fraternities. This incidence (18 per 1000) is approximately six times that (3·2 per 1000) in the general population of births (MacMahon *et al.*, 1953). Table II gives details of the fraternities in which a later sib was affected. Five of the six sibs were propositi in the series; the sixth was

TABLE I

INCIDENCE OF CONGENITAL HEART DISEASE IN SIBS BORN AFTER THE FIRST PROPOSITUS IN EACH FRATERNITY

First propositi		Subsequent sibs	
Nature of defect	Number	Number	Number with congenital heart disease
Transposition of the great vessels ..	28	24	1
Persistent common truncus arteriosus	15	17	0
Pulmonary stenosis	20	21	0
Coarctation of aorta..	22	20	0
Septal defects..	63	42	1
Patent ductus arteriosus	34	39	1
Other specified defects	33	26	0
Unspecified	202	153	3
Total	417	342	6

born in 1951, after the period covered by the enquiry. In three cases the diagnosis of congenital heart disease in the affected sib was confirmed post mortem; in the other three it rested on clinical examination (in one case accompanied by full investigation).

In three of the fraternities shown in Table II the specific nature of the cardiac defect was fairly reliably established in both affected: in two of them the first propositus and the affected sib exhibited the same abnormality (ventricular septal defect in one case, and complete transposition of the great vessels in the other). In the third fraternity the first propositus had a patent ductus arteriosus, and the sib showed transposition of the great vessels with ventricular septal defect. A specific congenital heart defect was also diagnosed in 2 of the 646 sibs born before the first propositus in each fraternity (both were born before the period of enquiry and are therefore not included among propositi). In one case the sib and propositus had a patent ductus arteriosus (both confirmed at operation): in the other the sib was examined clinically and thought to have a ventricular septal defect; the propositus exhibited Fallot's tetralogy (confirmed post mortem). Thus in three of five fraternities with two affected members in which the nature of the cardiac defect was known, the lesion was identical in both affected. The number of observations is of course very small, but this evidence suggests that the risk of recurrence of the same cardiac malformation may be greater than the risk of a different one.

The incidence of malformations other than congenital heart disease was not raised in sibs of propositi. Of the 1012 sibs, 9 exhibited other malformations, which were: anencephalus, spina bifida, harelip and cleft palate, absence of palate, aplasia of kidneys with talipes, absence of sternum,

TABLE II

DETAILS OF SIX FRATERNITIES IN WHICH A LATER SIB WAS AFFECTED

Birth rank	Sex	Date of birth	Fate	Diagnosis
1	M	20/4/40	Alive at 9 years	
2	F*	7/6/48	Died aged 3 weeks	Unspecified cardiac defect (clinical examination)
3	M*	20/6/49	Alive at 2 years	Fallot's tetralogy (full investigation)
1	F*	6/9/40	Died aged 7 weeks	Patent ductus arteriosus (P.M.)
2	F	31/12/42	Alive at 8 years	
3	F	12/1/44	Alive at 7 years	
4	M	20/1/45	Alive at 6 years	
5	M	10/10/46	Alive at 4 years	
6	F*	16/9/49	Died aged 3 months	Unspecified cardiac defect (clinical examination)
7	F	11/4/50	Died aged 2 days	Cause of death unknown
8	F	25/8/51	Alive at 5 weeks	
1	F*	7/5/42	Died aged 3 weeks	Unspecified cardiac defect (clinical examination)
2	F*	4/10/47	Alive at 4 years	Patent ductus arteriosus (clinical examination)
1	M*	30/1/43	Alive at 8 years	Patent ductus arteriosus (clinical examination)
2	F*	17/1/45	Died aged a few hours	Transposition of great vessels and ventricular septal defect (P.M.)
	F (twin)	17/1/45	Alive at 6 years	
3	M	10/6/50	Alive at 1 year	
1	F	6/4/45	Alive at 6 years	
2	F*	14/1/48	Died aged 3 months	Ventricular septal defect and marked cardiac hypertrophy (P.M.)
3	F*	25/11/49	Died aged 7 days	Ventricular septal defect (P.M.)
1	M	8/3/47	Died aged 3 days	Intracranial hæmorrhage (P.M.)
2	M*	12/11/49	Died aged a few hours	Complete transposition of great vessels (P.M.)
3	M	10/6/51	Died aged 13 days	Complete transposition of great vessels (P.M.)

* Propositus.

deaf mutism, Klippel Feil syndrome, and pseudo-hermaphroditism. This incidence (0·9%) is certainly no greater than that of malformations in the general population. It is of course possible that a few cases in stillbirths have been missed, but the number lost in this way must be small.

The mortality experienced by sibs appears not to have been raised. Among 997 sibs of propositi (excluding 15 confirmed or suspected cases of congenital heart disease from the original 1012) there were 32 stillbirths (32 per 1000 total births) and 51 infant deaths (53 per 1000 live births). The abortion rate experienced in the fraternities (propositi excluded) was 79 per thousand pregnancies. These rates are probably no higher than those prevailing in the general population of births during the same period.

It is unfortunately not possible to speak with confidence about the incidence of congenital heart disease in twins. There were 15 pairs of twins in the series, one with both members affected (both propositi), and 14 with one affected. But the 14 unaffected twins (of which 9 were alive at the time of investigation) were not examined, and the possibility that some of them were also affected cannot be excluded.

INCIDENCE IN COUSINS

Name and sex of all brothers and sisters of parents of propositi were recorded by field enquiry, as were the number and sex of their offspring. Suspected cases of congenital heart disease were noted. Fraternities (of first cousins of propositi) not well known to the person interviewed were excluded.

Of the 4143 cousins for whom a history was recorded, 25 were said to be affected. Inspection of hospital records confirmed the diagnosis in four cases, and refuted it in seven. Only one of the remaining 14 patients was available for clinical examination, and was found to be affected. It is of course quite possible that not all affected cousins were identified by relatives. But it seems certain that several of the 13 patients in whom the diagnosis was unconfirmed were unaffected, since of the 11 whose hospital records were traced, 7 were normal. Even if both confirmed (5) and unconfirmed (13) cases are included, the incidence in cousins (4·3 per 1000) is only a little higher than in the general population of births (3·2 per 1000).

Incidence in Parents

Data were recorded by field enquiry for 834 parents (424 mothers and 410 fathers). One mother refused to give the necessary information, and in 14 cases the child was illegitimate and the identity of the father unknown.

Fourteen parents were said to have congenital heart lesions. Twelve were examined clinically, when it was found that four had rheumatic heart disease and eight were normal. In the remaining two who were not examined the diagnosis had been made by a consultant physician and can probably be accepted: one of them (a mother) had a congenital heart block with some other lesion (probably a ventricular septal defect); and the other (a father) died of bacterial endocarditis with suspected congenital heart disease. In these two cases the specific nature of the defect in the propositus was not diagnosed. The incidence in parents (one or possibly two in 834) is possibly no higher than in the general population of adults, of which our only indication is the estimated incidence (1·1 per 1000) in children aged ten years (MacMahon *et al.*, 1953).

There were two first-cousin marriages (0·5%) among the 424 marriages of parents of propositi: in both cases the propositus exhibited dextrocardia and transposition of the viscera. There were seven patients with dextrocardia in the series, and the high incidence of consanguinity of parents in these cases provides support for Cockayne's suggestion (1938) that this condition may be inherited as a recessive.

There was one second-cousin marriage, which gave rise to a propositus with cor biloculare and atresia of the œsophagus.

Summary

The familial incidence of congenital heart disease was recorded for 425 fraternities which contained 431 propositi born to Birmingham mothers in the years 1940–49. There were six affected (18 per 1000) among 342 sibs born after the first propositus. This is approximately six times the incidence (3·2 per 1000) in the general population of births. The incidence of malformations other than congenital heart disease was not raised in sibs of propositi.

The nature of the cardiac defects was fairly reliably diagnosed in five fraternities with two affected members; in three of them the lesions were identical in both affected.

Five confirmed and 13 unconfirmed cases of congenital malformation of the heart were identified among 4143 first cousins of propositi. Of 834 parents, 14 were said to be affected. Further clinical examination indicated that eight of them were normal, four had rheumatic heart disease, and only two had congenital heart lesions.

There were two first-cousin marriages among 424 marriages of parents of propositi; in both cases the propositus exhibited dextrocardia and transposition of the viscera. In the series there were seven propositi with dextrocardia, and the high incidence of consanguinity provides support for Cockayne's suggestion that this condition may be inherited as a recessive.

For clinical records we are indebted to the staffs of all Birmingham hospitals, in particular of the Children's Hospital, and for post-mortem reports to Dr. H. S. Baar, Dr. W. Whitelaw, and other hospital pathologists. Dr. C. O. Carter, Dr. F. N. Elcock, and Dr. C. Papp provided hospital records of affected relatives.

We are particularly indebted to Miss M. S. Gradwell, who recorded family histories in the homes of patients.

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BALLISTOCARDIOGRAMS AFTER CIGARETTE SMOKING IN HEALTH AND IN CORONARY HEART DISEASE

BY

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It has long been known that smoking precipitates anginal attacks in certain patients subject to this disorder, but this occurs only rarely. Smoking also causes changes in the pulse rate and blood pressure of many people (Roth, 1951) and in the electrocardiogram of a few (Evans and Stewart, 1943; Graybiel *et al.*, 1938; and Wilson and Johnston, 1939), some subjects being unusually susceptible to the agent while others are affected little if at all.

Although it is agreed that if smoking precipitates cardiac pain the patient should not smoke, clinical experience with the effect of smoking on other cases of angina has not been sufficiently striking to make most doctors deprive their patients with coronary disease of this comforting habit; although, in the related arteriosclerotic condition of peripheral vascular disease the advice that such patients should stop smoking is now given routinely in many clinics. Because of the irregularity of the effect of nicotine on both healthy persons and those with cardiac disease, one is challenged to ascertain whether the heart of the patient before him is unusually susceptible to its effects or not, and to use this information as the basis for a decision regarding tobacco.

The ballistocardiograph has seemed particularly fitted to throw light on this problem, and it was employed for the purpose soon after instruments of this type became available in the clinic. Boyle *et al.* (1947) and Levy *et al.* (1946 and 1947) studied both the effect of smoking and of intravenous injection of nicotine itself on healthy persons and patients subject to coronary disease, using the Nickerson low frequency, damped ballistocardiograph (Nickerson, 1945) and making the more usual clinical measurements as well.

The results were irregular, some subjects of both healthy and cardiac groups showing marked changes of blood pressure, pulse rate, and the electrocardiogram after exposure to nicotine, but many others being affected little if at all. The cardiac output, calculated from the ballistocardiogram increased occasionally, but more often remained unchanged; and alterations in ballistic contour were not reported. The averages showed no significant difference between the circulatory dynamics of the response to nicotine in the two groups, but pain was produced in a few patients with coronary disease, and the electrocardiographic changes led to the conclusion that nicotine sometimes induced coronary insufficiency, either by coronary constriction or by increasing the work of the heart.

Using a different form of ballistocardiograph, the Dock portable direct-body type, Caccese and Schrager (1951) obtained more striking evidence of cardiac effects, for they demonstrated that changes of ballistic contour occurred after smoking in 18 of 31 subjects. Soon after, Mandlebaum and Mandlebaum (1952), using a ballistocardiograph of the same type, confirmed these results by finding that 28 per cent of 50 apparently healthy persons between 16 and 60 years of age, with normal ballistocardiograms before smoking, developed an abnormality of ballistic form after smoking, while in patients with coronary disease, most of whom had abnormal

*Working with a Nuffield Foundation Medical Fellowship

records before smoking, increased abnormality occurred after smoking more than twice as often as in healthy subjects. These results suggested that the effect of smoking on the heart was greater than the profession had believed; that patients with coronary heart disease were more frequently susceptible than had been realized; and that susceptibility and its absence could readily be detected by the ballistocardiogram and used as a basis for a decision whether a given patient should smoke or not. Indeed, making the decision in this way, the Mandlebaums (1952) were well impressed by the clinical result obtained by forbidding tobacco to those patients whose ballistocardiograms deteriorated after smoking.

It therefore appeared that investigators using two types of ballistocardiographs differing in their construction had obtained different results, one instrument recording a change of contour after smoking in many subjects, while the other failed to detect it, although there was ample evidence of other nicotine effects. Because of the obvious importance of the problem, it seemed wise to study a larger series of cases using a third type of ballistocardiograph, the high frequency table (Starr *et al.*, 1939), which has certain advantages over the other types. Therefore, experiments have been performed on the effect of cigarette smoking on 124 subjects, with results in general similar to those reported with the Dock-type instrument. So it seems evident that smoking produces, in a few persons judged to be healthy and in a much higher proportion of those having coronary disease, a striking though temporary change in the contour of the ballistocardiogram of a type readily judged abnormal because it is never seen in the records of healthy young adults.

Method and Material

Seven hundred and forty-four ballistocardiograms were taken on 124 subjects. Fifty of the subjects were healthy adults from 20 to 40 years of age, and thirty were healthy adults from 40 to 60 years of age; most were doctors, nurses, or hospital technicians, but also included were a few persons referred to the hospital and found to be healthy. Forty subjects were patients judged to have coronary disease because of a history of angina of effort or an electrocardiogram characteristic of cardiac infarction or both; these patients were drawn from the wards and outpatient clinics of the University of Pennsylvania Hospital, where all had had a complete clinical study. Because of the likelihood of the development of coronary disease in such cases—two patients with idiopathic hypercholesterolæmia, one with Buerger's disease, and one with diabetes mellitus with hypertension were also studied.

All the ballistic tracings were optically recorded on a high-frequency, undamped, table ballistocardiograph, and limb lead II of the electrocardiogram was simultaneously recorded to time and identify the ballistic waves. Standardization of the ballistocardiogram, by measuring the displacement of the base line caused by a force of 280 grams, was performed frequently. The standard adjustment was a displacement of the record's base line of 1 cm. by this force.

The test was conducted as follows. The subject came to the laboratory at least two hours after the last meal. After a rest period of at least 15 minutes the first ballistocardiogram was taken and at the end of the run the subject was asked to breathe deeply. The subject was then given a popular brand of American cigarette and told to smoke it in his accustomed manner, while he continued to lie on the table. After thus smoking for one minute, he desisted briefly while a second ballistocardiogram was taken and then continued smoking for four more minutes. Then a third ballistocardiogram was taken immediately, and a fourth, fifth, and sixth record at 5-minute intervals thereafter. Blood pressure was taken by the usual auscultatory method before each ballistocardiogram. The decision whether the patient inhaled or not was made both by observing him and asking his opinion.

The tracings were studied for gross changes in wave form, the heart rate was determined, and the height and breadth of the waves were measured. Cardiac force was estimated for all records and the Tanner formula (Tanner, 1949) was used to calculate the cardiac outputs of all records normal in form. The results were analysed statistically for significant differences between the

response of the normal subjects of the two age groups and the patients; and between the responses of those who inhaled the smoke and those who did not. As abnormalities of wave form were present in 34 of the 40 patients with coronary disease either before or during smoking, the cardiac output changes could be calculated in only 6 of these patients.

Results

Group A—Normal subjects between 20 and 40 years of age. Forty of this group inhaled the tobacco smoke and 10 did not. Table I shows the average percentage changes in heart rate, blood

TABLE I

Ballistocardiographic Changes Due to Smoking One Cigarette

	GROUP A				*GROUP B*				*GROUP C*			
	Inhaled smoke (40 subjects)		Did not inhale smoke (10 subjects)		Inhaled smoke (20 subjects)		Did not inhale smoke (10 subjects)		Inhaled smoke (33 subjects)		Did not inhale smoke (7 subjects)	
	Mean	S.D. of mean	Mean	S.D. of mean	Mean	S.D. of mean	Mean	S.D. of mean	Mean	S.D. of mean	Mean	S.D. of mean
Heart rate	+17·2%	±1·9	+2·7%	±1·1	+6·6%	±2·1	+1·9%	±0·8	+12·2%	±2	−0·4%	±1·2
Systolic B.P.	+5·4%	±1·2	+1·8%	±2·4	+5·2%	±0·9	−3·4%	±1·5	+4·6%	±1·5	+1·7%	±1·5
Diastolic B.P.	+7·2%	±1·4	+1·8%	±2·5	+8·2%	±0·4	−0·7%	±2	+5·5%	±1·8	+2·5%	±1·3
Cardiac output/min. ..	+13·7%	±1·9	−0·4%	±1·7	+2·2%	±3·6	−1·9%	±2·1	+2·5%	±2·5	−9%	±4·5
Cardiac strength ..	−1·9%	±2	−2·7%	±3	−6·1%	±2·7	−12·3%	±3·3	−9·8%	±3·2	−10·5%	±3·7
Wave form change ..	0%		0%		15%		10%		39%		28%	
Increased IJ respiratory variation	32·5%		10%		30%		20%		45%		43%	

Group A consists of 50 healthy persons aged 20–40 years. Group B, 30 healthy persons aged 40–60 years, and Group C patients with coronary heart disease. The figures given in the " form change " and " increased respiratory variation " columns are the percentages of the number in that group showing such ballistocardiographic changes.

pressure, cardiac force, and cardiac output and the standard deviations of the means both in those who inhaled and in those who did not. The resting ballistocardiogram of each subject was normal, and in no cases did the record become abnormal in form after smoking. In 14 subjects (28%) there was an increase in the respiratory variation of the ballistic waves, illustrated by Fig. 1A, which doubtless accompanied the deeper breathing that occurs during smoking.

Group B—Normal subjects between 40 and 60 years of age. Of the 30 persons in this group, 20 inhaled and 10 did not. Table I shows the average percentage changes in heart rate, blood pressure, cardiac force, and cardiac output and the standard deviations of the means. All the initial ballistocardiograms were normal in form, but four subjects developed abnormalities of form after smoking. In three of the four positive tests the subjects, all of whom inhaled the smoke, experienced tingling of the extremities, nausea, and vertigo, so that the unduly severe cardiac response was accompanied by other manifestations of unusually severe nicotine action. An example of the change of wave form is shown by Fig. 1B. In 8 persons (27%) including the four who developed wave abnormalities, there was an increase in the respiratory variation of the ballistocardiogram after smoking.

Group C—Subjects with coronary heart disease. Of this group, 33 inhaled the tobacco smoke and 7 did not. Table I shows the average percentage changes in heart rate and blood pressure of the whole group, and the changes in cardiac force and cardiac output and the standard deviations of the means in the 6 patients (all inhalers of smoke) whose values could be calculated from the records. The initial ballistocardiograms of 19 patients were normal and 21 were abnormal. Ten of the 19 patients with normal initial tracings developed abnormalities of form, and 5 of the 21 patients with abnormal initial tracings developed more severe abnormalities after smoking. Thirteen

of the 15 patients with positive tests inhaled the smoke. Fig. 1C and all the tracings in Fig. 2 illustrate the records obtained. An increase in the respiratory variation developed in 13 of the 15 patients with positive tests and in an additional 5 patients who showed no change in wave form after smoking.

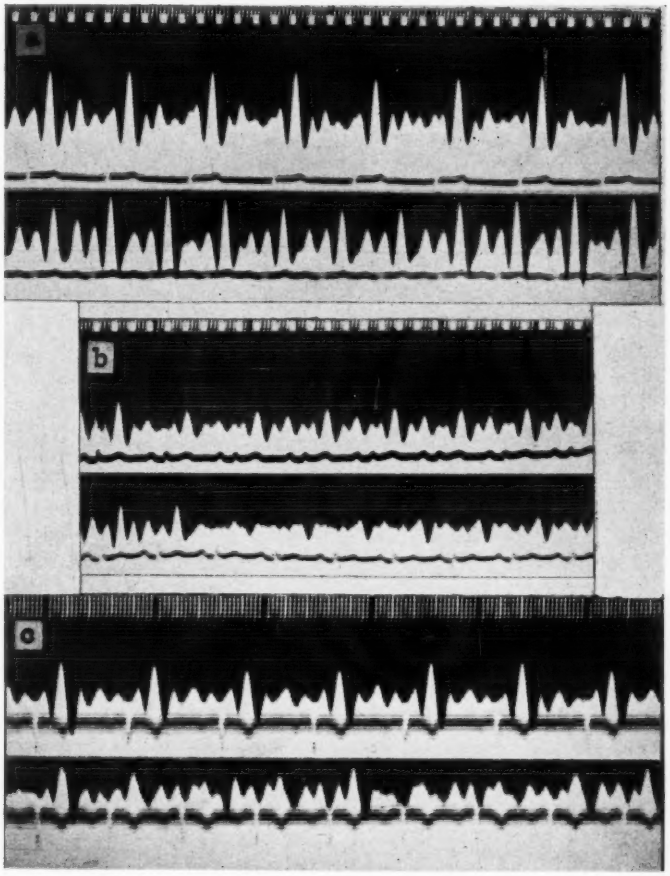

FIG. 1.—The effect of smoking on the ballistocardiogram with lead II cardiogram. The time record is at the top of each set of tracings and applies to the two records below. The time interval between the thick black lines is 1 second. The tracings are natural size. (a) R.S., aged 32 years. Normal cardiovascular system. BP. 125/70; heart rate 72/min.; E.C. normal. Upper control record is normal. Next record taken immediately after the subject has been smoking for 5 minutes; BP. 140/85; heart rate 102/min. Record normal, but IJ respiratory variation increased. (b) C.P., aged 44 years. Normal cardiovascular system. BP. 120/80; heart rate 80/min.; E.C. normal. Upper control record is normal. Next record after smoking for 5 minutes; BP. 140/100; heart rate 90/min. Record abnormal; I small and J small and deformed in the expiratory complexes. The IJ respiratory variation is increased. (c) R.B., aged 45 years. Angina of effort for 4 months. BP. 105/70; heart rate 70/min.; E.C. normal (the inversion of the cardiogram shown is due to incorrect lead attachments). Upper control record is normal. Next record after smoking for five minutes; BP. 110/80; heart rate 86/min. Record abnormal; complexes irregular in form, I small and frequently above the base line and J tiny and deformed in the expiratory complexes. The IJ respiratory variation is increased. The tracing, taken 15 minutes after smoking in each case, was normal and has not been reproduced.

Group D—Miscellaneous cases. This group consisted of two patients with idiopathic hypercholesterolæmia who were considered otherwise healthy, one patient with Buerger's disease, and one with diabetes mellitus and hypertension. The initial ballistocardiogram of the case of Buerger's disease was abnormal, those of the other cases were normal. After smoking, each of the patients showed deterioration of wave form. Fig. 3A and 3B illustrate the records taken from the cases of hypercholesterolæmia and Fig. 3C from the case of Buerger's disease.

Effects due to inhaling the smoke. The data given in Table I show that changes in the cardiovascular dynamics occurred among those who inhaled the smoke, to a degree not found in those who did not inhale, as was certainly to be expected. This was true of all the groups studied, although the type and degree of change varied somewhat from group to group. In the healthy young persons, Group A, the average increase in pulse rate and estimated cardiac output was significantly greater in those who inhaled, but the blood pressure changes were not significantly different. In those older, healthy persons, Group B, the averages differed in the same direction, but the differences were not statistically significant. Again, in the coronary heart disease group, Group C, the average increase in heart rate was significantly higher in the smoke inhalers, but the blood pressure differences were not significant. Obviously, those who were judged to inhale the smoke exhibited greater responses to smoking than those judged not to inhale it.

Alteration of ballistic size. When the ballistocardiogram was normal in form the effect of smoking on its amplitude was not conspicuous in the young people, but amplitude diminished after smoking in both the older, healthy subjects, and the coronary group. The average diminution in the estimate of cardiac strength based on the vertical I–J distance (Starr *et al.*, 1950) gives evidence of this. The increase of cardiac output as estimated from the ballistocardiogram was conspicuous only among the smoke inhalers of the younger group, and the changes found there were due to changes in heart rate.

Alteration in ballistic contour. When such alterations occurred after smoking, they were usually very conspicuous, as Fig. 1, 2, and 3 show clearly. Detailed description of a ballistic abnormality of form is never easy because the contour so often changes from beat to beat within the respiratory cycle, nevertheless, several types deserve attention. In the 23 tests in which ballistic form became abnormal after smoking, the systolic ballistic waves were affected in several combinations.

FIG. 2.—The effect of smoking on the ballistocardiogram. Record slightly reduced in size. (a) J.A., aged 45 years. Angina of effort for two years. BP. 160/80; heart rate 72/min.; E.C. normal. Upper control record is abnormal—I is tiny and slurred during expiration and the IJ respiratory variation is abnormally large. Next record after smoking for 5 minutes; BP. 180/90; heart rate 86/min. Record more abnormal—nadir of I above the base line and J tiny and deformed. (b) W.S., aged 54 years. Angina of effort for 3 years. B.P. 170/105; heart rate 82/min.; E.C. normal. Upper control record is abnormal—J waves are deformed and H waves equal the J waves in height in some small complexes. Second record after smoking for 5 minutes; BP. 170/95; heart rate 110/min. Record more abnormal—H waves are much larger and the J waves more deformed. Third record, 15 minutes after smoking; BP. 180/100; heart rate 104/min. Record still grossly abnormal. (c) C.D., aged 39 years. Angina of effort for 6 months and known hypertensive for 6 years. BP. 220/120; heart rate 84/min.; E.C. abnormal. Upper control record abnormal—I waves small. Next record after smoking for 5 minutes; BP. 240/130; heart rate 110/min. Record more abnormal—H and I waves smaller and K waves larger. The tracings taken 15 minutes after smoking in (a) and (c) had reverted to the control form and have not been reproduced.

FIG. 3.—The effect of smoking on the ballistocardiogram. Record slightly reduced in size. (a) J.B., aged 39 years. Idiopathic hypercholesterolæmia—blood cholesterol 620 mg. Normal cardiovascular system. BP. 100/60; heart rate 66/min.; E.C. normal. Upper control record is normal. Next record after smoking for 5 minutes; BP. 115/70; heart rate 68/min. Record abnormal—H wave increased in height and J wave smaller than H, and deformed in some complexes. (b) F.F., aged 30 years. Idiopathic hypercholesterolæmia—blood cholesterol 700 mg. Normal cardiovascular system. BP. 120/80; heart rate 74/min.; E.C. normal. Upper control record is normal. Next record after smoking for 5 minutes. BP. 125/80; heart rate 78/min. Record abnormal—I waves smaller during expiration, and the IJ respiratory variation is abnormally large. (c) C.M., aged 25 years. Buerger's disease for 3 years. Amputation of right great toe. BP. 150/95; heart rate 92/min.; E.C. abnormal. Upper control record is normal. Second record after smoking for 5 minutes. BP. 170/100; heart rate 120/min. Record grossly abnormal—I waves small, and J waves small and deformed during expiration. Third tracing, 15 minutes after smoking; BP. 150/95; heart rate 104/min. Tracing still grossly abnormal. The tracings taken 15 minutes after smoking in (a) and (b) had reverted to normal and have not been reproduced.

A combination of I and J wave abnormalities occurred in 10 cases of coronary disease, 4 normal subjects in the 40 to 60 age group, the one with Buerger's disease, and one with idiopathic hypercholesterolæmia. The abnormalities consisted of a decrease in the depth of the I wave, in some complexes the nadir of the wave being above the base line, and a decrease in height and deformity of the J wave. The changes were greatest in the small expiratory complexes. Examples of these abnormalities are shown in Fig. 1B and C, 2A, and 3B and C.

A combination of H and J wave abnormalities occurred in four cases of coronary disease, one with idiopathic hypercholesterolæmia, and in the one with diabetes mellitus. There was an increase in the height of the H wave as measured from the base line and the J waves became deformed or smaller than the H waves in some of the expiratory complexes. These types of abnormalities are illustrated by Fig. 2B and 3A.

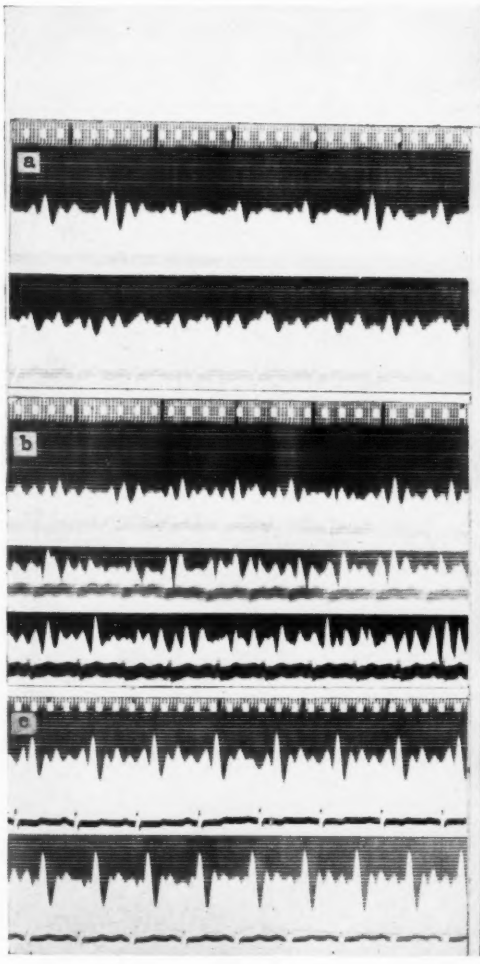

FIG. 2

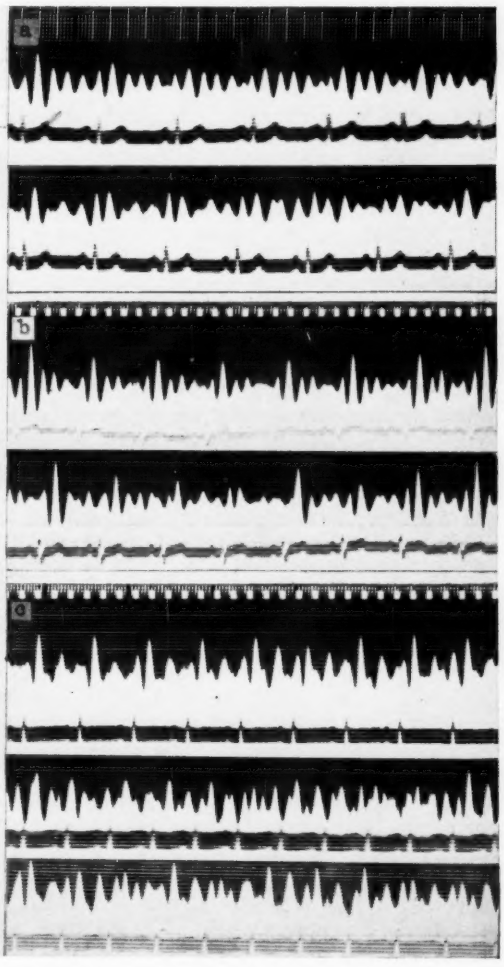

FIG. 3

A combination of H, I, and K wave abnormalities occurred in one patient with coronary heart disease and hypertension. In all phases of respiration the H and I waves decreased and the K wave increased in size (Fig. 2C).

Duration of the abnormalities after smoking. In most cases the form of the ballistocardiogram reverted to its pre-smoking state within 5 minutes after the cessation of smoking. In a few instances, however, the abnormalities persisted longer than 15 minutes as shown by Fig. 2B and 3C.

Discussion

The results show clearly that smoking a single cigarette has a temporary influence on the myocardial function of certain persons, as judged by the contour of the ballistocardiogram. Healthy persons under 40 are not thus affected, although the increased heart rate, the average significantly greater than in older persons, indicates that nicotine was indeed exerting its usual action. In older persons, however, even though they seemed healthy, this myocardial effect is seen occasionally, and in those with coronary heart disease it is seen in about one-third of the cases. The few patients tested who, without symptoms or signs suggesting coronary disease, were suffering from conditions in which coronary disease is a frequent complication, all showed abnormality of myocardial function after smoking. Obviously, therefore, tobacco exerts an effect on the myocardium more frequently in those with coronary disease than in healthy persons; the difference is statistically significant in my data.

The nature and significance of this effect deserves discussion. Abnormal ballistic patterns of the type encountered after smoking have never been seen in records from the hundreds of healthy young adults who have been tested in this laboratory. Patterns resembling those seen after smoking have been encountered in persons suffering from advanced heart disease as diagnosed by the usual clinical criteria. It seems likely, therefore, that the effect of tobacco on the myocardium of the susceptible subject must be regarded as deleterious.

Smoking is well known to increase respiration, blood pressure, and heart rate, and it is proper to ask the question whether the myocardial effect detected could be secondary to any of these changes. The evidence is against this possibility. Every subject was asked to take a deep breath at the end of his control tracing and in no instance were abnormalities of contour, similar to those seen after smoking, encountered. Nor is there any regular relation between these abnormalities and blood pressure or pulse rate changes. The deterioration of wave form was associated with an increase in heart rate and blood pressure in 11 of the 23 positive tests, with no change in six tests, with an increase of blood pressure alone in four tests, and with an increase in heart rate alone in two tests.

The ballistic waves that deteriorated in form after smoking are in most cases those associated with cardiac contraction and ejection of blood into the great vessels, i.e. H, I, and J. waves, thus suggesting a change in the character of contraction and of ejection. The evidence indicates that this change is not solely the result of an increase of cardiac work, which overtaxes myocardial capacity, as six subjects with positive tests had no change in heart rate or blood pressure when the waves became abnormal, and in several others the ballistocardiogram reverted to normal when the heart rate and blood pressure were still elevated; nevertheless, it should be pointed out that increase in calculated cardiac output per minute, or increase in blood pressure, or both, did accompany the ballistic abnormality in many instances, so increased heart work might often have been a factor in producing a relative ischæmia.

A more probable primary mechanism is that of coronary vasoconstriction. This conception is supported by the character of the abnormalities of electrocardiographic wave form produced occasionally by smoking (Wilson and Johnston, 1939) which is often similar to that frequently seen in patients with cardiac infarction, and can be produced in animals whose coronary circulation has been interrupted. Coronary constriction was not demonstrated after nicotine in the older

animal experiments designed to test the point (Sollman, 1948), and this is also true in still unpublished data (Eckenhoff, personal communication) secured by more modern methods (Eckenhoff *et al.*, 1947). The results of the experiments of Burn (1951) indicate, however, that smoking leads to an outpouring of pituitary hormones which are well known to produce coronary vasoconstriction. This evidence therefore supports the view that coronary vasoconstriction is the explanation of the cardiac effects seen after smoking in my subjects.

But whatever the exact mechanism, the incidence of myocardial abnormality after smoking found in patients with coronary heart disease is far greater than that found in healthy persons in the older age group; this difference is statistically significant, and it indicates that pre-existing coronary artery disease enhances the deleterious effect of smoking on cardiac contraction. Fifteen of the subjects who had positive smoking tests had coronary heart disease and the remaining 8 were either in the 40 to 60 age group or suffered from diseases well known to predispose towards coronary heart disease, e.g. idiopathic hypercholesterolæmia, Buerger's disease, and diabetes mellitus. It is interesting to speculate whether in the latter eight patients the effect of nicotine exposed a latent coronary artery disease.

In the present series of cases, tobacco smoking adversely affected cardiac function in 38 per cent of the people with clinical evidence of coronary heart disease. If, as Mandlebaum and Mandlebaum (1952) have reported, the symptoms of such patients are considerably improved by abstention from smoking, then the result of this test is important in deciding the subsequent management of the patient.

Summary

A study has been made of the effect of smoking a single cigarette on the cardiovascular dynamics of healthy persons and of patients with evidence of coronary heart disease, using a high-frequency ballistocardiograph.

In 50 healthy young persons, although there was a considerable increase in average pulse rate after smoking, the form of the ballistocardiogram remained normal in every case.

In 30 older persons believed to be healthy, a temporary abnormality of the ballistocardiogram followed smoking in 4 instances.

In 40 patients with clinical evidence of coronary heart disease, the ballistocardiogram became abnormal or more abnormal in form after smoking in 15, or 38 per cent. In four patients without clinical evidence of coronary heart disease, but suffering from diseases in which coronary heart disease is a frequent complication, smoking caused ballistic abnormalities in all.

Unusual cardiac sensitivity to nicotine is readily detected by the ballistocardiogram, and it is found more frequently in cardiac patients than has been generally realized. The significance of this finding is discussed.

I am deeply indebted to Dr. Isaac Starr, Professor of Therapeutic Research, University of Pennsylvania Hospital, Philadelphia, U.S.A., for his guidance during the year I worked in his laboratory and for the considerable assistance which he gave to me in the preparation of this paper.

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CONGENITAL TRICUSPID ATRESIA

BY

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Many papers have been written on the diagnosis and prognosis of tricuspid atresia. Differences between various descriptions, especially in papers on X-ray features, may be explained partly by the rarity of the condition and partly by the effects produced by other complicating anomalies. Tricuspid atresia is responsible for only about 5 per cent of all cyanotic heart disease in infancy, and many patients die in the first few months of life. Consequently it is unlikely that any one centre will quickly collect a large series of cases and it may be of value to describe our findings in 15 patients with tricuspid atresia and one with congenital tricuspid stenosis. We are grateful to colleagues who have referred these patients to us for investigation.

As advocated by Edwards and Burchell (1949), we have attempted to classify our cases into those with and those without associated transposition of the great vessels, and have subdivided these two groups according to the presence or absence of pulmonary (or sub-pulmonary) stenosis. The importance of recognizing these associated abnormalities early has been stressed by Kroop (1951), who points out that a child who has tricuspid atresia, without transposition but with pulmonary stenosis, has a 66 per cent chance of dying in infancy; and that it is the child with precisely this combination of defects who best responds to operative treatment. Gasul *et al.* (1949) have given practical support to this view by obtaining successful anastomosis, even in very young infants, by using Potts's modification of the Blalock-Taussig operation.

The abnormalities that have been disclosed in our cases are summarized in Table I. Dr. H. S. Baar has kindly provided us with necropsy reports. Although anatomical records of similar accuracy cannot be obtained in the living subject, angiocardiography allows the atrial septal defect to be seen clearly and we have assumed transposition to be present when the pulmonary artery fills early and directly from the left ventricle. We have not accepted inadequate and/or delayed filling of the pulmonary artery as evidence of pulmonary stenosis, for this also occurs in the absence of stenosis when the pulmonary artery originates from a vestigial right ventricle. The methods have provided sufficient information to allow us to divide our cases into 7 with transposition (3 of whom had pulmonary stenosis) and 9 without transposition (3 with pulmonary stenosis, 3 with normal pulmonary arteries, and 3 not determined). We observed no example of pulmonary atresia and the ductus may well have been patent in more cases than we recognized. One child (M.A.) had an extraordinary heart, which will be described in detail in a separate paper; the vestigial right ventricle emptied into a hypoplastic pulmonary artery and was in communication not only with a hypertrophied left ventricle but also with a third ventricular chamber which lay under the skin of the abdominal wall.

Clinical Findings

Taussig (1936 and 1947) has given a succinct account of the symptoms and signs of tricuspid atresia. We can add nothing to her descriptions and therefore confine our comments to certain more controversial features.

Cyanosis was early apparent (Table II) and was sometimes present at birth, but we have been unable to confirm the statement by Gasul *et al.* (1950) that early and intense cyanosis suggests

TABLE I

NATURE OF ANATOMICAL DEFECT

	Patient	Evidence	Right ventricle	Left ventricle	Pulmonary artery	Aorta
			With Transposition			
(*a*)	D.C.	N	Vestigial	Large	From LV. Stenosed	From RV. Large
	R.O'S.	N	Small	Large	From RV. Stenosed	From RV. PDA.
	C.L.	A	Vestigial, fills late		From LV. Poor flow	From LV
(*b*)	C.H.	A	Not seen		From LV. Fills early	From RV. Fills late
	P.T.	N	Small	Large	From LV	From RV
	B.S.	A	Vestigial, fills late		From LV. Good flow	From RV. Fills late
	L.B.	A	Vestigial, fills late		From LV	From RV
			Without Transposition			
(*a*)	M.A.	N	Vestigial. Subumbilical extension	Large	From RV. Stenosed	From LV
	M.O'N.	N	Vestigial	Large	From RV. Stenosed	From LV
	P.D.	N	Small, tricuspid stenosis	Intact VS	From RV. Stenosed	From LV
(*b*)	J.O.	N	Vestigial	Large	From RV	From LV. PDA.
	J.S.	N	Vestigial	Normal	From RV	From LV
	J.F.	N	Small	Large	From RV	From LV
(*c*)	J.H.	A	Not seen		? From RV. Poor flow, fills late	From LV
	D.D.	A	Not seen		? Origin. Poor flow	From LV
	P.M.	A	Not seen		? From RV. Poor flow, fills late ? Large bronchial arteries	From LV

Abbreviations: LV, RV=left and right ventricles. VS=ventricular septum. PDA=patent ductus arteriosus. N=Necropsy. A=Angiocardiogram.

All patients have an atrial septal defect, usually with enlargement of both atria. All except the child with tricuspid stenosis have a ventricular septal defect.

tricuspid atresia without transposition. In fact transposition was absent in the only infant who was never cyanosed: she died of heart failure at the age of five weeks, but at no time was she blue. Children who survived long enough developed finger and toe clubbing. Moderate polycythæmia was common. Four children (C.L., M.O'N., J.F., and D.D.) had spontaneous attacks of unconsciousness; three of these had radiological evidence of pulmonary oligæmia and one (C.L.) would draw himself into the knee-elbow position during attacks of dyspnœa. Only one child squatted; his lung vessels were congested. Dyspnœa was almost always a feature and, in those who were old enough to walk, exercise tolerance was severely limited.

Congestion and prominent *pulsation in the neck veins* was a valuable diagnostic sign, but hepatic engorgement was sometimes more readily recognized in infants. When considering differential diagnosis it is well to remember that striking pulsation of the neck veins may occur in patients with pulmonary stenosis and an intact interventricular septum. Peripheral œdema was recorded three times and splenic enlargement twice.

Heart Size. We failed to confirm the impression (Gasul *et al.*, 1950) that infants with transposition have bigger hearts than those without transposition; indeed, we were unable to discover any method by which to distinguish clinically between patients with and without transposition. Nor were we able to determine from history and physical signs whether children had pulmonary plethora or oligæmia. We did notice that by our clinical methods we tended to underestimate the size of the heart. While murmurs were usual, they were not invariable. They were

TABLE II

MAIN CLINICAL FEATURES

Classification	Patient	Sex	Diagnosis at age	Confirmed by*	First cyanosed	Neck veins	Lung fields (X-ray)	Heart size (clinical)	Electrical axis
			With Transposition						
(*a*) Pulmonary stenosis	D.C.	M	8 mo.	N	Birth	+	Oligæmic	Normal	—
	R.O'S.	F	2 mo.	N	Birth	+	Oligæmic	+	L
	C.L.	F	3	A	4 mo.	+	Oligæmic	+	L
(*b*) No stenosis	C.H.	F	10*	A	3 mo.	—	Normal	Normal	L
	P.T.	M	2	N	3 mo.	Normal	Congested	+	R
	B.S.	M	6	A	3 mo.	Normal	Normal	Normal	L
	L.B.	F	8	A	3 mo.	+	Congested	+	L
			Without Transposition						
(*a*) Pulmonary stenosis	M.A.	F	18 mo.	N	1 mo.	+	Oligæmic	+	L
	M.O'N.	F	12 mo.	N	6 mo.	—	Oligæmic	+	L
	P.D.†	M	1 wk.	N	3 days	—	Oligæmic	+	—
(*b*) No stenosis	J.O.	F	1 mo.	N	Not blue	+	Congested	+	—
	J.S.	F	2 mo.	N	1 mo.	Normal	Oligæmic	Normal	—
	J.F.	M	2 mo.	N	Birth	+	Normal	+	—
(*c*) Undetermined	J.H.	M	11	A	10 days	+	Oligæmic	+	L
	D.D.	M	18 mo.	A	2 mo.	+	Oligæmic	+	L
	P.M.	M	4	A	Birth	+	Oligæmic	+	L

* Died one year later: no necropsy. † Tricuspid stenosis. N=Necropsy. A=Angiocardiogram.

commonly systolic, rough, best heard in the third intercostal space close to the sternum, and sometimes audible at the back of the chest between the scapulæ. Our attempts to gain useful information from an analysis of the second sound at the base of the heart were unsuccessful. Blood pressure readings were within the normal range.

ELECTROCARDIOGRAPHY

Electrocardiograms were taken in 11 patients (Fig. 1) and we agree with other writers that left ventricular preponderance or marked left axis deviation in cyanotic heart disease is almost diagnostic

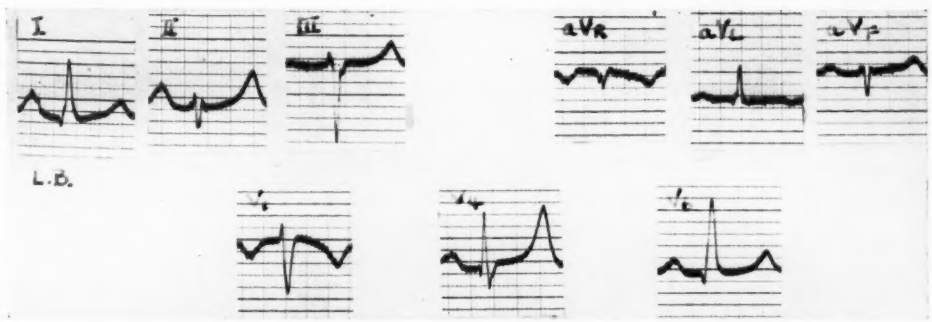


FIG. 1.—Typical electrocardiogram showing left ventricular preponderance as was seen in all the cases except one.

X

of tricuspid atresia with a rudimentary right ventricle. One of our patients had left bundle branch block, which is unusual.

It is widely recognized that left axis deviation and cyanosis may occur in other conditions, and we have seen the combination in Eisenmenger's complex, complete transposition of the great vessels, single ventricle with persistent truncus arteriosus communis, and in a child whose cyanosis was due to methæmoglobinæmia. Gasul *et al.* (1950) have recorded similar findings in Ebstein's disease and in patients whose great veins open into the left atrium; Donzelot *et al.* (1950) mention a case of infantile coarctation with cyanosis and left axis deviation.

Records of right ventricular preponderance or right axis deviation from patients with tricuspid atresia are less common (Kroop and Grishman, 1950). One of our patients (P.T.) showed this phenomenon in a minor degree (Fig. 2): unfortunately no chest leads were obtained. The child died suddenly during right heart catheterization and the diagnosis of tricuspid atresia with rudimentary right ventricle and transposition of the great vessels was confirmed at necropsy. No satisfactory explanation could be advanced to account for the electrocardiographic findings nor for the unexpected death.

FIG. 2.—An unusual electrocardiogram showing the absence of left axis deviation, but unfortunately, chest leads were not available.

RADIOLOGY

The X-ray picture of tricuspid atresia is said to be characteristic, and has been described as follows.

In the frontal projection. (1) Diminished pulmonary vascular markings (except when there is an associated transposition of the great vessels).

(2) Concavity of the left middle segment.

(3) Prominent left lower segment—" long and convex " (Eek, 1949); " well rounded " (Brown, 1950); " unusual . . . a blunt and false apex high above the diaphragm " (Wittenborg *et al.*, 1951).

In the left anterior oblique position. (1) A prominent posterior border, requiring considerable rotation to clear the spine (a large left ventricle).

(2) Little or no forward projection (small or absent right ventricle).

Various other features have been added to this generally accepted description of the characteristic pattern. For example, Taussig (1947) mentions that the shadow of the great vessels is narrow and does not increase in width when the patient is rotated into the left oblique position. She also describes dilatation of the superior vena cava as a sign evident in early infancy, and increased lung vascularity when there is associated transposition. In the frontal projection Gasul *et al.* (1950) note that the border of the heart extends only slightly to the right of the spine; Brown (1950) says that the right border has an exaggerated convexity, but others (Cooley *et al.*, 1950; Wittenborg *et al.*, 1951) speak of diminished convexity or even concavity. Eek (1949) points out that both atria are large, and Snow (1952) talks of paradoxical pulsation of the anterior and posterior borders when the heart is viewed in the left anterior oblique position.

Wittenborg *et al.* (1951) found that only 2 of their 11 cases had the " characteristic " radiological appearances, and suggested that right atrial enlargement, due to smallness of the atrial septal defect, often obscured the hypoplasia of the right ventricle. Most of their cases were indistinguishable from Fallot's tetralogy.

We also have felt dissatisfied with the usually accepted X-ray features and, in order to try to discover more reliable diagnostic signs, we have compared the features outlined in the preceding paragraphs with those seen in our patients (Fig. 3). The cases divide themselves into two distinct groups from the radiologist's point of view, according to the degree of vascularity of the lung fields.

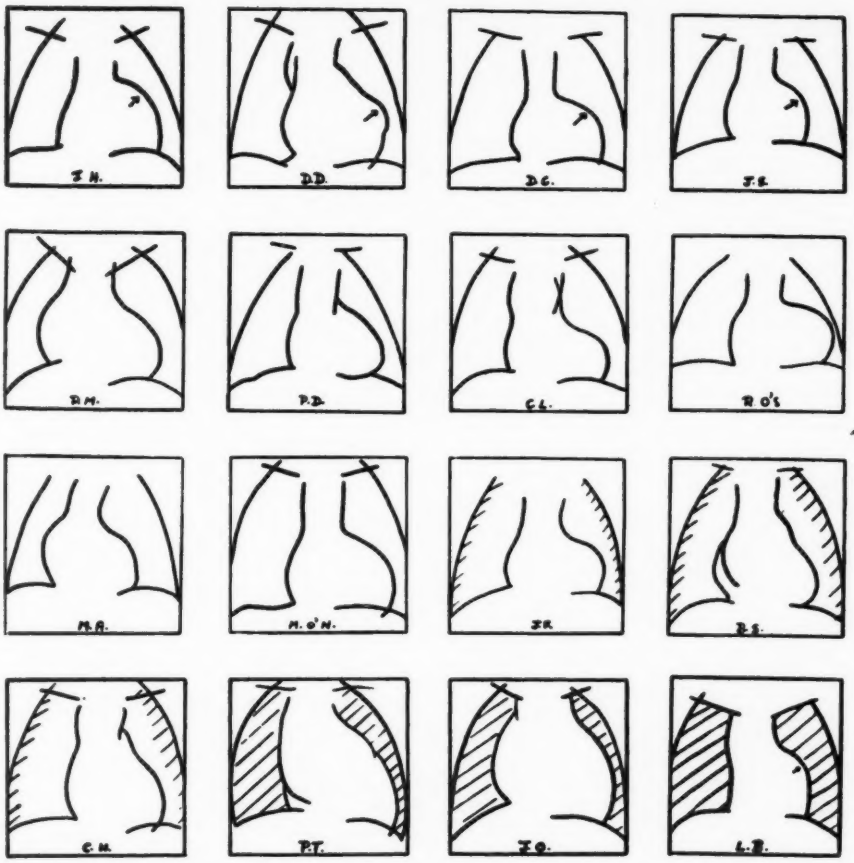


FIG. 3.—The cardiac silhouettes of 15 children with tricuspid atresia and 1 child with tricuspid stenosis. (Clear lungs indicate pulmonary oligæmia; partial shading means normal vascularity and complete shading pulmonary plethora.)

GROUP 1. REDUCED PULMONARY VASCULARITY (10 CASES, 3 WITH TRANSPOSITION)

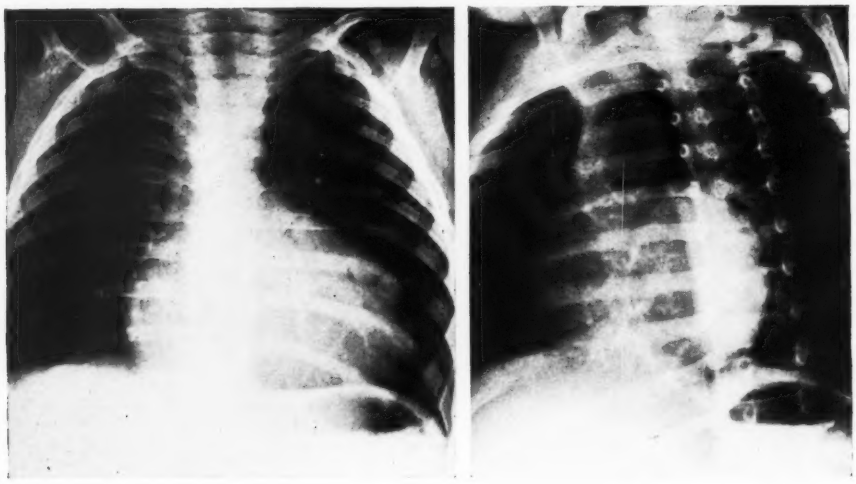
(A) Frontal Projection

The *left middle segment* was concave in 9 and flat in 1 child and probably indicates either a misplaced (i.e. transposed) pulmonary artery or one carrying little blood. The latter may occur when there is pulmonary stenosis or sometimes when an artery of normal size originates from the rudimentary right ventricle.

The *left lower segment* was unusual in shape in 5 of the 10 children. Its lower part ran a long and vertical course and its upper part was remarkably prominent and angulated. This gave the heart a somewhat square shape (Fig. 4). In the other 5 children there was a tendency to the same configuration although in two it was much less definite.

The shadow of the *great vessels* was narrow in 7 cases, but only once to a striking degree. This child (D.C.) had complete transposition of the great vessels.

The *right border* of the heart extended only slightly to the right of the spine in 7 patients. It sometimes showed a flatter curve than usual.

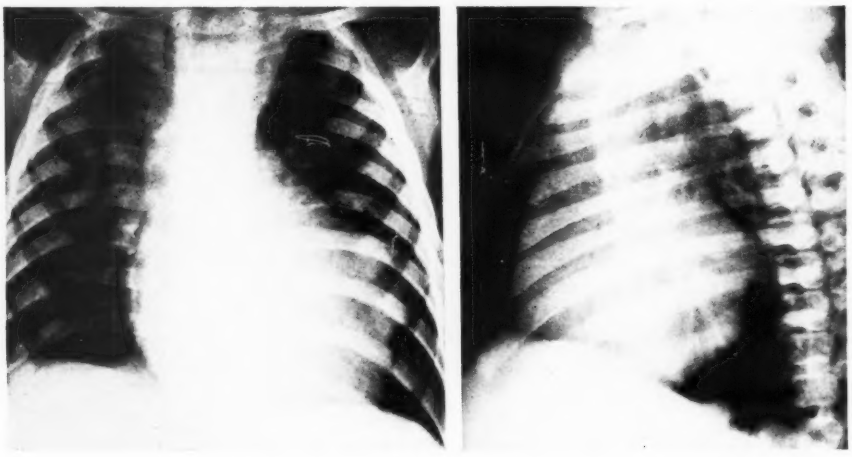


A B

FIG. 4.—(A) The " square " heart shape in the frontal view. There is a prominence in the upper part of the lower segment of the left border, below a concave pulmonary segment. Other features in this child are pulmonary oligæmia, a rather narrow great vessel shadow and the slight cardiac extension to the right of the spine. (B) The " square " appearance in the left oblique view. The same child as in Fig. 4 A. Both the left atrial and the left ventricular segments of the posterior border are prominent. The anterior border is not prominent.

(B) Left Anterior Oblique Projection

The prominence of the *posterior border,* not only in its lower (left ventricular) segment but also higher up towards the tracheal bifurcation in the left atrial segment, made the heart somewhat square, with an appearance akin to that noted in the frontal projection (Fig. 4 and 5).



A B

FIG. 5.—(A) Another example of the " square " shape. In this child the prominence on the left border constitutes a separate segment. (B) The " square " appearance in the left oblique view, corresponding to Fig. 5 A. The left atrial and left ventricular prominences posteriorly are distinct.

The projection of the *anterior border* varied from flat to normal but was never increased.

As we have not looked specifically for *paradoxical pulsation* in most of these children we cannot here assess its importance.

(*C*) *Right Anterior Oblique Projection*

A barium swallow gave no indication of left atrial enlargement in the four children examined.

Group II. Normal or Increased Pulmonary Vascularity (6 Cases; 4 with Transposition)

(*A*) *Frontal Projection*

The *left middle segment* was sometimes concave, sometimes prominent.

In the *left lower segment*, only one child's heart had the square shape seen in Group I. Two hearts were not enlarged and one of these was almost normal in shape; another was large and globular with no specific features to suggest a diagnosis.

Narrowing of the shadow of the *great vessels* was observed once; the child had a right-sided aortic arch.

Four of the six patients showed only slight extension of the *right border* of the heart shadow to the right of the spine. In one child this border was slightly concave.

On two occasions the *left atrium* could be seen through the heart shadow as a rounded area of increased opacity.

(*B*) *Left Anterior Oblique Projection*

Posterior border. The square shape described in Group I was observed only once, in the child already mentioned who had a similar appearance in the frontal view. In another child there was gross backwards and downwards bulging of the left ventricular segment. Another child had no apparent left ventricular enlargement.

The child with the square heart presented a flat *anterior border.* Two children had a forward bulging of the upper part of the border, probably right atrial in origin. In one of these there was a notch anteriorly just above the diaphragm, presumably at the point of junction with a hypoplastic right ventricle.

(*C*) *Right Anterior Oblique Projection*

Five children were examined. The œsophagus was displaced by considerable left atrial enlargement in one child; there was slight enlargement in two, possibly slight enlargement in one and no enlargement in the fifth.

Discussion of Radiological Findings

Although the lung fields are usually oligæmic, clearly this is not an essential nor even a characteristic feature of the X-ray appearance. And when the lungs are congested it does not necessarily mean that there is associated transposition of the great vessels; we have seen congested lungs in the absence of transposition, and oligæmia in its presence.

In view of Wittenborg's (1951) difficulty of distinguishing tricuspid atresia from Fallot's tetralogy, we have particularly compared our findings in the present series with those of 41 children with the latter condition.

Frontal projection. The most striking differential feature in the frontal projection appears to be the shape of the left heart border. In tricuspid atresia, concavity of the pulmonary segment, together with prominence in the upper part of the left lower segment and a vertical border below this, can give a square shape to the heart that we have not seen convincingly demonstrated in any other condition. Amongst the 41 cases of Fallot's tetralogy only three had any suggestion of this configuration and in none was it definite.

Most of the children showed only slight cardiac extension to the right of the spine in the frontal position. But as 13 of the 41 with Fallot's tetralogy also showed minimal projection, we cannot regard this sign by itself as an indication of a small right ventricle. Nevertheless, when associated with a suggestive appearance of the left heart border, its presence increases the probability of the diagnosis.

In the frontal projection, various other signs, sometimes absent, may be accepted as similar corroborative evidence although they do not of themselves have great diagnostic value. These features include narrowness of the vascular pedicle and a flat or concave lower right heart border.

Left anterior oblique view. In this position, 17 of the 41 children with right ventricular hypertrophy due to Fallot's tetralogy had an X-ray appearance that exactly fitted the usually accepted description of tricuspid atresia, i.e. there was slight or no anterior cardiac projection but considerable posterior bulging. Consequently we feel that we cannot accept this appearance as evidence of a hypoplastic right ventricle. We have found as a more reliable and characteristic feature of tricuspid atresia a moderate posterior projection that involves not only the lower (left ventricular) segment but also the upper (left atrial) part of the posterior border. The segments may be clearly separated by a groove and the resultant appearance is a square shape somewhat akin to that presented in the frontal view. In a few children really gross bulging of the left ventricular segment may make the left atrial prominence less obvious, with loss of the " square " shape; but the posterior bulge of the heart then becomes directed backwards and downwards, in contrast to the purely posterior bulge of the displaced and rotated left ventricle in Fallot's tetralogy.

Tricuspid atresia is excluded if, in this position, the interventricular groove can be seen in its normal position. Considerable prominence of the anterior border excludes tricuspid atresia, but a normal amount of forward projection, or even exaggerated prominence, providing it is confined to the upper (right atrial) segment, is not inconsistent with the diagnosis. A flat anterior border, a notch anteriorly just above the diaphragm, or paradoxical pulsation as described by Snow (1952) are additional corroborative signs of tricuspid atresia.

Right anterior oblique view. We observed left atrial enlargement, detectable by barium swallow, only in children not presenting the square shape and only in those with normal or increased pulmonary vascularity. Sometimes the enlarged chamber was more evident in the frontal projection as an opacity seen through the heart. Although the appearance is not pathognomonic we believe that, if the patient is cyanosed and the lung vessels full, the finding of a large left atrium even in the absence of any other abnormality should suggest the possibility of tricuspid atresia.

Explanation of the square heart. The cardiac apex can be elevated and rounded by enlargement of either ventricle (Fig. 6) but perhaps left ventricular hypertrophy is more liable to affect the upper part of the left lower segment. However, we do not believe that left ventricular enlargement alone is sufficient to account for the square heart which is such a characteristic feature in some cases of tricuspid atresia, especially when the lungs are oligæmic.

In 1951 Janker and Hallerbach, using ciné-angiocardiography, pointed out that in tricuspid atresia the left atrial appendix usually showed clearly, whereas it was rarely visible in Fallot's tetralogy. In one of our patients (Fig. 5A), the angular part of the left heart border was formed by a distinctly demarcated segment and angiocardiograms showed the prominence to be due to the left atrial appendix (Fig. 7A). There were similar findings in another child, and we suggest that the square configuration of the heart is due to a prominent left atrial appendix below a concave pulmonary segment.

In the left oblique view the square shape depends on a bulge in the upper part of the posterior border. Angiocardiograms show that this prominence also is atrial and that the chamber seems to be displaced upwards.

Curiously enough, despite this evidence of left atrial prominence in two projections, none of the children with a square heart has shown deviation of the œsophagus when examined in the right anterior oblique position; such deviation has been confined to those *not* showing the square configuration. This seems to contradict Schwedel's (1946) rule that the smooth walled atrium enlarges before

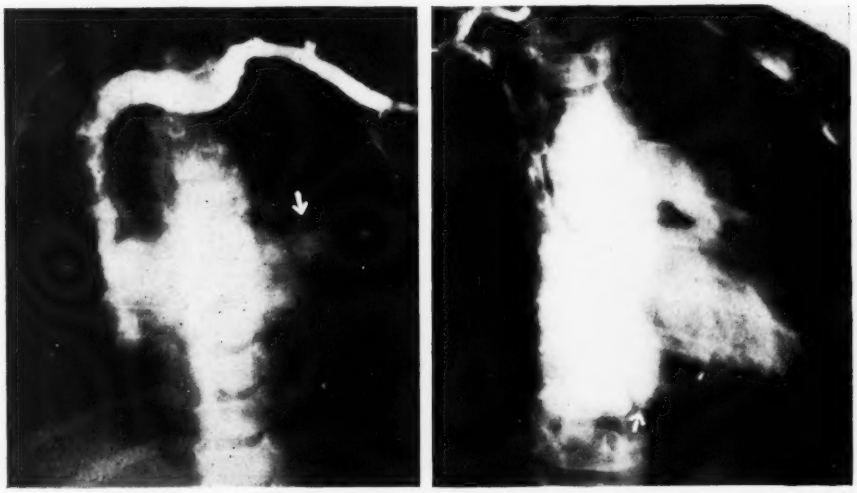
its trabeculated appendix, but the contradiction may be more apparent than real. Janker and Hallerbach (1951) believe that left ventricular hypertrophy, when associated with a rudimentary right ventricle, may cause cardiac rotation and so make the appendix of the left atrium readily visible. We agree with these observations and believe that the prominence of the left atrial appendix in tricuspid atresia is often due rather to altered anatomical relationships than to the degree of enlargement.

FIG. 6.—The left heart border in right and left ventricular enlargement. (*a*) Right ventricular enlargement (Fallot's tetralogy). (*b*) Left ventricular enlargement (chronic hypertension; no cardiac abnormality except left ventricular hypertrophy shown at necropsy). The cardiac apex is elevated and the left lower segment rounded in both infants.

From our analysis we conclude that direct X-ray examination can indicate the diagnosis in a considerable proportion of cases, especially when the lungs are oligæmic. Recognition of the anomaly is much more difficult when they are normal or plethoric.

ANGIOCARDIOGRAPHY

Seven children were examined by angiocardiography. The main feature in each case was the flow of diodone from the right to the left atrium in the early pictures. Instead of the normal U-shape of the right heart in the frontal position, the two atria formed a continuous band of opacity with a well defined horizontal upper margin that extended from the right heart border across the mid-line towards the left. Meanwhile the position normally occupied by the right ventricular inflow tract, just above the diaphragm to the left of the mid-line, was conspicuously empty (Fig. 7A). Both these features were emphasized by Campbell and Hills (1950).



A B

FIG. 7.—(A) Early angiocardiogram film, corresponding to Fig. 5. There is a flow of diodone from the right atrium to the left atrium while the area normally occupied by the right ventricular inflow tract is empty. The prominence of the left heart border in the straight radiograph is seen to be due to the left atrial appendix (arrow). (B) Angiocardiogram later in the series. (Not the same child as in Fig. 7A.) From the left atrium diodone has entered the left ventricle and both great vessels have filled immediately (transposition of pulmonary artery only). Later, a rudimentary right ventricle has filled (arrow).

The left ventricle filled from the left atrium. The rudimentary right ventricle was recognized late in the series on three occasions in the position normally occupied by the right ventricular inflow tract (Fig. 7B).

In four patients the aorta, lying in its normal position, filled immediately from the left ventricle. In three of these filling of the main pulmonary arteries was delayed or not seen, and we concluded that the arteries were arising from a rudimentary right ventricle. The fourth child showed immediate filling from the left ventricle of both the aorta and the main pulmonary artery, indicating transposition of the pulmonary trunk only. All four had poor filling of the peripheral lung vessels, corresponding to the oligæmic appearance recognized on direct examination.

In the remaining three children aortic filling was delayed, whereas the main pulmonary artery filled immediately from the left ventricle. The pulmonary blood flow, estimated by the filling of the peripheral parts of the pulmonary arterial tree, was good and corresponded to an appearance of normal or increased lung vascularity on direct examination. We concluded that these children had complete transposition of the great vessels.

Angiocardiography proved useful to confirm the diagnosis; it gave information about the size of the atrial defect and—sometimes by inference—about the origin of the great vessels; it gave potentially valuable pre-operative evidence concerning the size and position of the pulmonary arteries.

Prognosis and Treatment

Our findings are essentially the same as those of previous workers. If the lungs are oligæmic it is likely that the pulmonary artery is arising from the rudimentary right ventricle or, if transposed to the left ventricle, that it is stenosed. In either case death is likely to occur in infancy. Four of our five patients with pulmonary stenosis died early and two of these infants had transposition. When a pulmonary artery of normal calibre is transposed to the left ventricle, the pulmonary blood flow is increased and the prognosis is much more favourable (Hedinger, 1915). This state of affairs is suggested radiologically by congested lungs, and in such cases it is pointless to try to improve the condition by surgical methods designed to increase pulmonary flow.

We do not accept Gasul's (1950) suggestion that, in tricuspid atresia, operation should be confined to those infants who have pulmonary stenosis without transposition. Discussing the treatment of patients with complete transposition of the great vessels (without tricuspid atresia) we suggested that associated pulmonary stenosis improved the prospects of a successful anastomotic operation (Astley and Parsons, 1952). Much the same arguments apply to children with transposition, pulmonary stenosis, *and* tricuspid atresia. Unsaturated blood entering the right atrium flows to the left atrium and thence, mixed with oxygenated blood returning in small quantity from the lungs, enters the left ventricle. Blood escapes with difficulty through the stenosed, transposed pulmonary artery to the lungs, but passes more readily through the ventricular septal defect to the rudimentary right ventricle and aorta. By anastomosing an aortic branch to a pulmonary artery the flow of blood to the lungs is increased and consequently more oxygenated blood returns to the heart. The work of the left ventricle and the volume of blood passing through right ventricle, aorta, and coronary arteries is but little changed. However, the blood is better oxygenated so that all organs supplied by the aorta must benefit including, of course, the myocardium.

We therefore consider that, in tricuspid atresia, providing the atrial septal defect is large enough to allow a good flow of blood from right to left, demonstration of pulmonary oligæmia is the sole criterion needed before advising thoracotomy. In view of the poor prognosis, operation should be performed as soon as possible after confirmation of the diagnosis and, since the vast majority of patients are likely to be infants, Potts's operation is to be preferred to the Blalock-Taussig anastomosis. Results of operation vary. The immediate mortality is higher than in pulmonary stenosis. After successful operation great improvement is to be expected, but, because there is only one functioning ventricle, it is unlikely ever to be so remarkable as that obtained in Fallot's tetralogy.

SUMMARY

Fifteen cases of tricuspid atresia and one of congenital tricuspid stenosis have been examined. The combination of distended, pulsating neck veins with a cardiogram showing left axis deviation is almost diagnostic, but exceptions are noted. Methods of differentiating associated cardiac malformation are considered in view of the influence of these factors on diagnostic features and on prognosis. Radiological appearances are reviewed and fresh diagnostic criteria are suggested. Results of angiocardiography are given and the selection of patients for operation is discussed.

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LEFT ATRIAL AND PULMONARY CAPILLARY VENOUS PRESSURES IN MITRAL STENOSIS

BY

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A method of measuring pulmonary " capillary " pressure by wedging a catheter into a terminal branch of a pulmonary artery was introduced by Hellems *et al.* in 1948. To differentiate this from pressures recorded in a blocked pulmonary vein (e.g. through an atrial septal defect) this pulmonary " capillary " pressure will be referred to as pulmonary capillary venous pressure (P.C.V.P.), following the lead of Lagerlöf and Werkö (1949). Subsequent investigations have produced conflicting evidence concerning the interpretation and accuracy of such pressure measurements, and this report presents the results of a new method used to investigate the relationship between P.C.V.P. and left atrial pressure.

Dow and Gorlin (1950) found a close correlation between P.C.V.P. and left atrial pressure in dogs; the two pressures also varied directly under abnormal conditions. Several investigators have found the P.C.V.P. to be higher than the pressure in the left atrium, considerably so in some instances (Hellems *et al.*, 1948, 1949; Lagerlöf and Werkö, 1949; Calazel *et al.*, 1951; and Ankeney, 1952). Ankeney has recently questioned whether phasic variations in P.C.V.P. records reflect similar phasic pressure changes in the left atrium, and suggests that the true P.C.V.P. is essentially devoid of phasic variations. Opinion among investigators also varies with regard to the significance and interpretation of the waves seen in P.C.V.P. tracings.

So far all published attempts to record pressures from a blocked pulmonary artery and from the left atrium simultaneously have been in dogs under general anæsthesia or in human subjects with atrial septal defect. In this investigation the problem has been tackled in the conscious human subject in the absence of a septal defect. Certain patients with mitral valve disease were selected for this study, in view of the practical importance of measuring the P.C.V.P. in that condition.

It is common knowledge that the tracheal bifurcation and left atrium are in close proximity, and that an enlarged left atrium in mitral valve disease may widen the carina and compress the left main bronchus. Post-mortem examinations confirmed the fact, first demonstrated by Allison (1952) in this country, that a needle could be introduced through the left main bronchus into the left atrium without endangering any nearby vital structure.

Method. After studying relevant anatomy in the cadaver, a No. 22 gauge needle, 5 cm. long, was selected for the left atrial puncture. The needle was attached to the distal end of a metal bronchoscopic suction tube. A polythene catheter inside the metal tube connected the needle to the recording machine. Fig. 1 illustrates the position of a three-way tap that provided the essential means of recording immediately consecutive pressures from the left atrium and from a blocked peripheral pulmonary artery.

Cardiac catheterization was performed by the standard method of Cournand on the conscious patient 30 minutes after oral administration of 3 grains of sodium amytal and 0·5 grains of codeine phosphate. Heparin, 5000 units (50 mg.), was injected through the catheter. Pressures were recorded in mm. Hg. by means of a Sanborn electromanometer and a direct writing multichannel

* Work undertaken during the tenure of a fellowship from the Dazian Foundation for Medical Research, U.S.A.

oscillograph with simultaneous electrocardiogram. Mean pressures were obtained by electrical integration of the oscillograph tracings. An adjustable mechanical damper was used to eliminate artefacts in the pressure records. The zero point for all pressures was the sternal angle.

The pulmonary artery pressure and P.C.V.P. were recorded under resting conditions and the catheter then withdrawn to a main branch of the pulmonary artery. Blood samples were taken simultaneously from the brachial artery and pulmonary artery, and the oxygen content measured by the method of Van Slyke. The oxygen consumption was then estimated by means of a closed circuit spirometer.

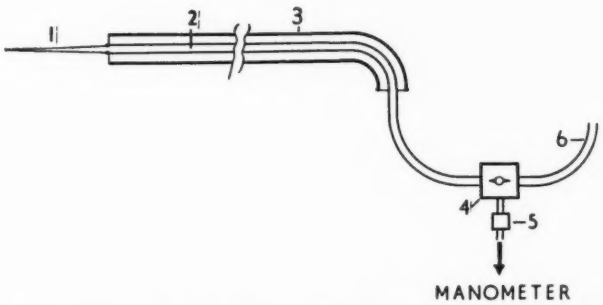

FIG. 1.—Arrangement of apparatus to record immediately consecutive P.C.V.P. and left atrial pressure (see text). (1) Needle in left atrium. (2) Polythene catheter. (3) Metal bronchoscopic suction tube. (4) Three-way tap. (5) Mechanical damper. (6) Intracardiac catheter to blocked peripheral pulmonary artery.

The patient was prepared for bronchoscopy by an amethocaine lozenge and topical amethocaine (2%) to the pharynx and larynx while on the catheter table. A Negus bronchoscope was then introduced, the patient remaining supine on the table. The exact site of needle puncture was settled in advance after studying the radiological anatomy of the left atrium, carina, and left main bronchus, and was confirmed by direct inspection: the point selected lay between 1 and 5 mm. distal to the carina on the medial wall of the left main bronchus. When the atrium was small, the more distal area was chosen and the needle was directed somewhat medially; but this was not necessary when the atrium was large and the carinal angle wide. By inserting the needle about half-way between the anterior and posterior walls of the left main bronchus, the pulmonary artery anteriorly and the œsophagus posteriorly were avoided.

After passing the bronchoscope, the manometric zero point was readjusted to sternal angle level and the catheter was again advanced until it blocked a peripheral pulmonary artery. When a satisfactory P.C.V.P. tracing was obtained, the bronchoscopy needle was flushed with saline and then pushed through the bronchial wall into the left atrium, and this position was at once confirmed by recording a left atrial pressure curve. In all instances the left atrium was easily entered.

Using the three-way tap, pressure tracings were obtained from the left atrium and from a blocked peripheral pulmonary artery in immediate succession without pause. Electrical mean pressures were recorded from both sites in the same way, and these procedures were then repeated while the patient stopped breathing at the resting respiratory level. The needle and bronchoscope were then withdrawn.

RESULTS

Pressure measurements and relevant clinical data are recorded in Table I. Cases 4 and 5 represent examples of high pulmonary artery pressure and increased pulmonary arteriolar resistance (Fig. 2 and 3). A normal pulmonary artery pressure and pulmonary arteriolar resistance were

TABLE I

PULMONARY CAPILLARY VENOUS PRESSURES AND LEFT ATRIAL PRESSURES

Case No.	Age and sex	Diagnosis	Resting state before bronchoscopy						Bronchoscope in position			
			P.A.P.		P.C.V.P.		Cardiac output (Litres/min.)	Pulmonary arteriolar resistance (Dynes sec. cm.$^{-5}$)	P.C.V.P. S/D	L.A.P. S/D	P.C.V.P. M	L.A.P. M
			S/D	M	S/D	M						
1	42 F	M.S., A.S. and A.I., N.R.	22/14	16	11/7	8	6·8	94	20/16	22/14	16	16
2	46 F	M.S., N.R.	52/25	35	25/18	20	4·3	279	27/18	25/22	19	18
3	44 M	M.S., T.S., Aur. Fibr.	24/15	20	10/8	9	3·4	259	9/7	9/6	9	9
4	34 F	M.S., Aur. Fibr.	75/38	52	35/20	25	3·1	697	36/22	36/22	27	27
5	40 F	M.S., Aur. Fibr.	110/60	75	33/28	30	2·8	1,288	23/14	25/13	18	18
6	42 M	M.S. and M.I., A.S., Aur. Fibr.	27/13	20	19/10	13	3·3	169	30/11	30/11	15	15
7	39 F	M.I., Aur. Fibr.	21/11	16	20/8	13	2·2	109	33/11	30/11	17	17

All pressures recorded in mm. Hg.

P.A.P. =Pulmonary arterial pressure.
P.C.V.P. =Pulmonary capillary venous pressure.
L.A.P. =Left atrial pressure.
S/D =Systolic and diastolic pressures.
M =Mean pressure.
M.S. and M.I. =Mitral stenosis and mitral incompetence.
T.S. =Tricuspid stenosis.
A.S. and A.I. =Aortic stenosis and aortic incompetence.
N.R. =Normal sinus rhythm.
Aur. Fibr. =Auricular fibrillation.

Pulmonary arteriolar resistance is calculated from the Poiseuille equation, $\text{Resistance} = \frac{\text{Pressure gradient}}{\text{Rate of blood flow}}$, and is expressed in dynes second cm^{-5} (Gorlin, 1951).

found in Cases 1, 6, and 7. Passive pulmonary hypertension and a slight increase of pulmonary arteriolar resistance were found in Case 2. Case 3 was of special interest because of the catheter demonstration of a previously undiagnosed tricuspid stenosis, which was presumed to be partly responsible for the relatively low pulmonary artery pressure and P.C.V.P. (Fig. 5). The mean left atrial pressure and P.C.V.P. agreed closely in each case regardless of the pressure level recorded.

All P.C.V.P. tracings showed venous pulse waves similar in form to those recorded directly from the left atrium. In the two cases with sinus rhythm typical *a* and *v* waves were recorded from both sites (Fig. 4). Auricular fibrillation was present in five cases. In these there were no *a* waves but good *v* waves were seen in both sets of tracings, each resembling its counterpart very closely in form and amplitude. Left atrial pressure pulses showed small *c* waves regardless of the rhythm, but these were less evident in P.C.V.P. records (Fig. 3A, 6, and 7).

All pressure waves obtained from a blocked peripheral pulmonary artery showed a delay of from 0·02 to 0·08 sec. when timed in relation to corresponding waves from the left atrium.

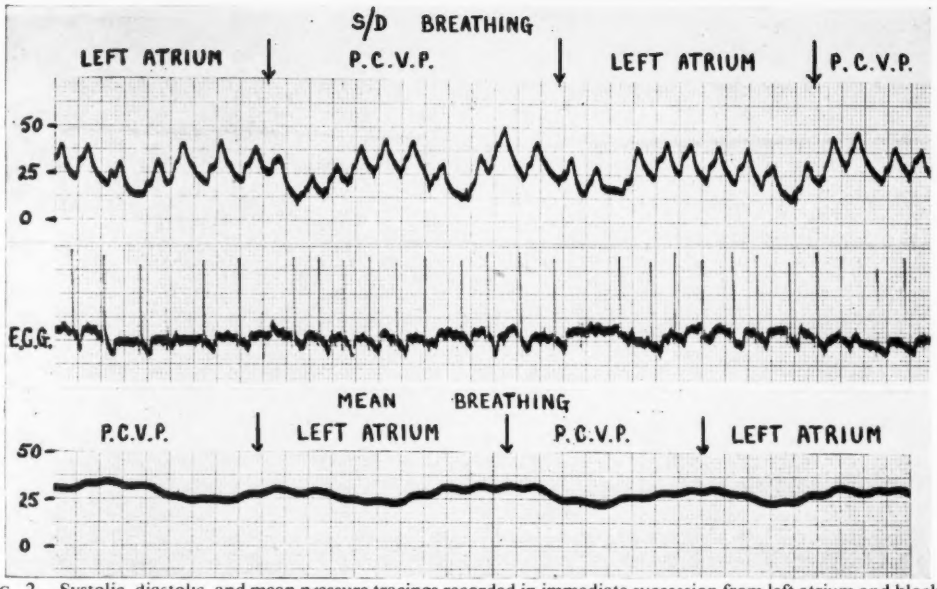

FIG. 2.—Systolic, diastolic, and mean pressure tracings recorded in immediate succession from left atrium and blocked peripheral pulmonary artery. The equality of the pressures is shown. Note the undulating pressure fluctuations related to breathing. Instant of tap switch is marked by arrow. Paper speed 10 mm. a second (Case 4).

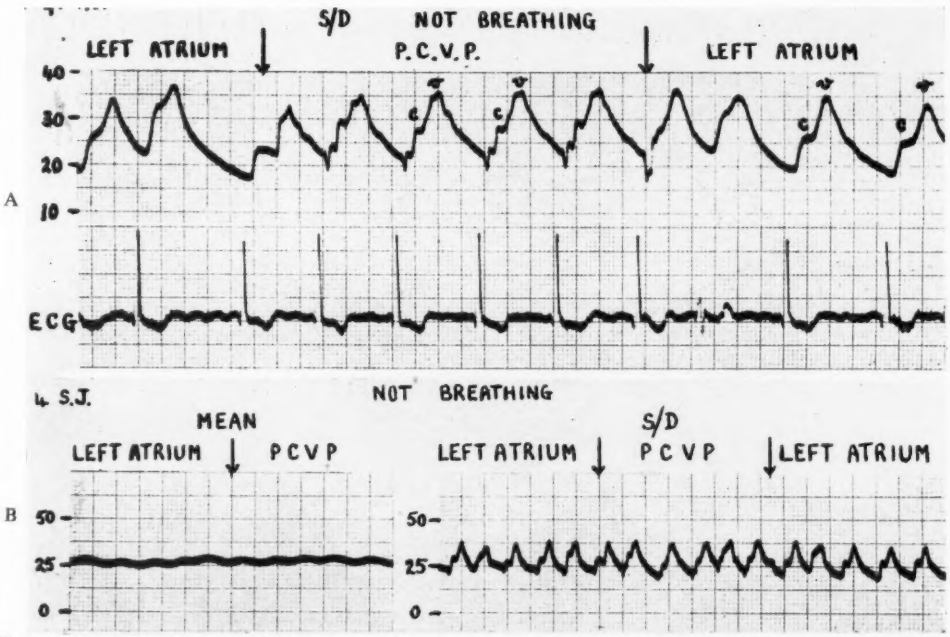

FIG. 3.—(A) Record of immediately consecutive pressure tracings in auricular fibrillation, showing similarity of venous wave pattern (see text). Instant of tap switch is marked by arrow. Paper speed 25 mm. a second (Case 4). (B) Immediately consecutive pressure records in a case with auricular fibrillation showing equal systolic, diastolic, and mean pressures in blocked peripheral pulmonary artery and left atrium. Instant of tap switch is marked by arrow. Paper speed 10 mm. a second (Case 4).

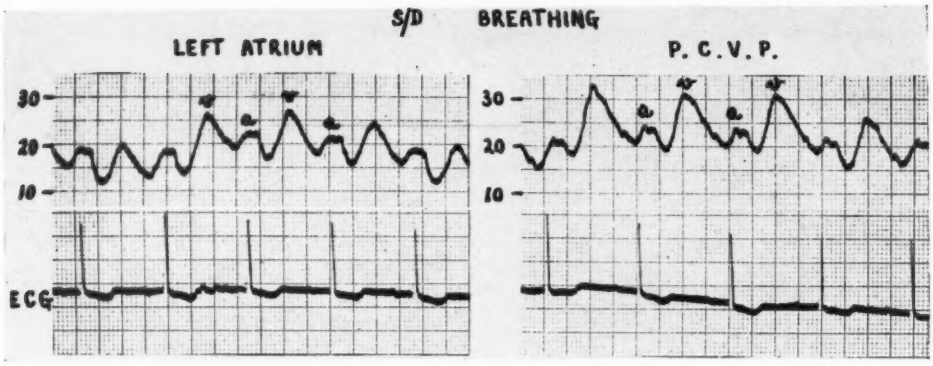

FIG. 4.—Pressure tracings from blocked peripheral pulmonary artery and left atrium with sinus rhythm to show similarity of venous pulse wave (see text). The pressures are not immediately consecutive. Paper speed 25 mm. a second (Case 2).

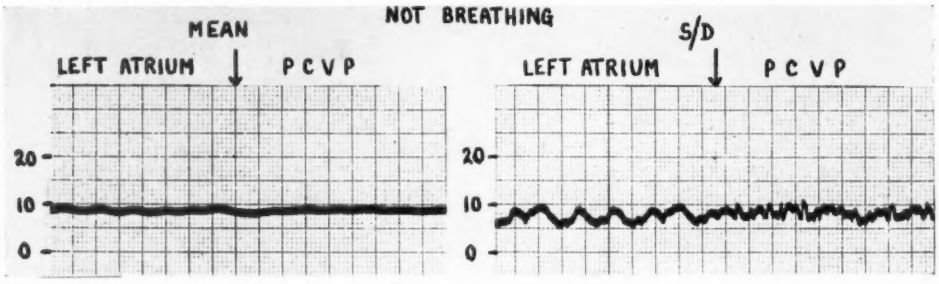

FIG. 5.—Immediately consecutive pressure tracings from blocked peripheral pulmonary artery and left atrium in a case with auricular fibrillation showing identical pressures. This is the only case with a P.C.V.P. venous pulse wave that was not shown clearly (see text). Instant of tap switch is marked by arrow. Paper speed 10 mm. a second (Case 3).

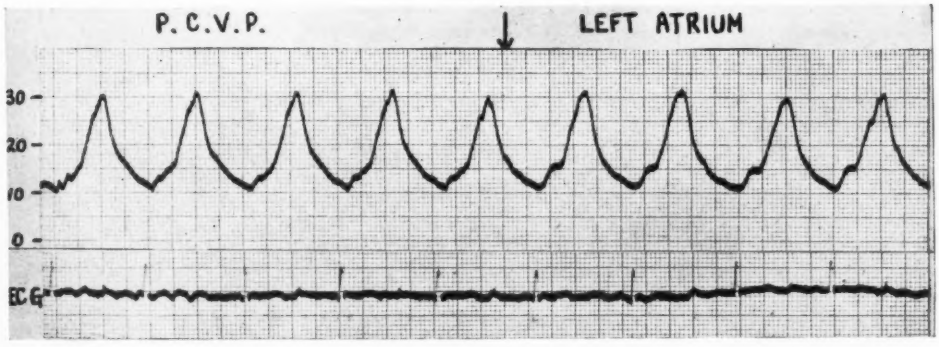

FIG. 6.—Immediately consecutive pressure record from left atrium and blocked peripheral pulmonary artery in mitral stenosis and regurgitation with auricular fibrillation to show similarity of pressure and wave pattern. Instant of tap switch is marked by arrow. Paper speed 25 mm. a second (Case 6).

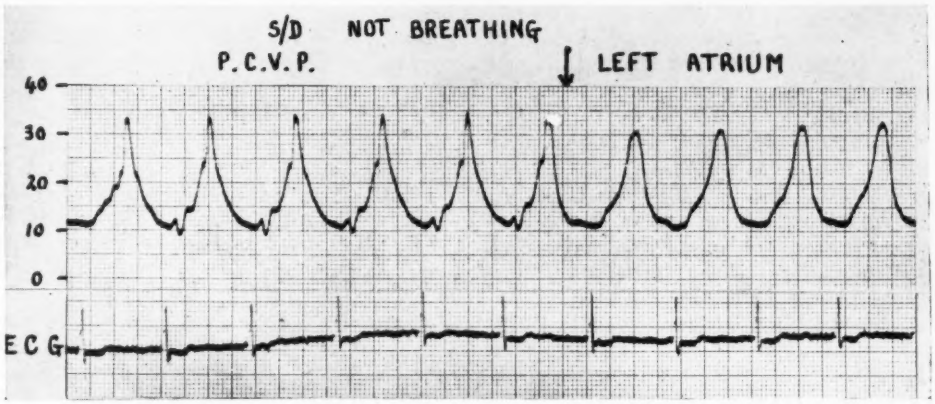

FIG. 7.—Immediately consecutive pressure tracing from left atrium and blocked peripheral pulmonary artery in mitral incompetence with auricular fibrillation showing the type of venous pattern recorded. The mean pressures were identical (see text). Instant of tap switch is marked by arrow. Paper speed 25 mm. a second (Case 7).

DISCUSSION

For the purpose of this study, cases were specially selected to include examples of sinus rhythm, auricular fibrillation, low and high left atrial pressures, and low and high pulmonary arteriolar resistances. One case of pure mitral incompetence was included.

We have been greatly impressed by the marked lability of the left atrial pressure and P.C.V.P. in relation to the phases of respiration and to minor variations in the resting physiological state of the patient. Misleading figures could easily be obtained in comparing these two pressure records unless simultaneous or immediately consecutive tracings were taken. In general there was a considerable rise in P.C.V.P. during insertion of the bronchoscope, followed by a slow return to the resting level.

Proper damping is essential in obtaining accurate pressure curves. Although some difficulty in this respect was encountered, since accurate tracings had to be recorded from two different sites and through two different systems in rapid succession, critical damping was achieved in most instances (Fig. 3 and 6). Mean pressures were not subject to damping errors and gave convincing proof that P.C.V. and left atrial pressures were identical in all the cases studied.

From previous catheter studies in mitral stenosis carried out in this department, it has long been maintained that a proper P.C.V.P. tracing should be venous in form (Wood, 1952), and the evidence now presented shows clearly that these waves are derived from the left atrium (Fig. 4). In the presence of auricular fibrillation there can be no *a* wave but only Mackenzie's ventricular form of the venous pulse, the *v* wave (Fig. 3 and 6).

Despite proper blocking of a peripheral pulmonary artery by the catheter the typical venous wave pattern may not be present. A low or normal pressure in the left atrium may be associated with *a* and *v* waves of such low amplitude that they cannot be detected in the P.C.V.P. tracing, presumably because of the damping effect of the intervening capillaries. Extreme pulmonary vaso-constriction in certain cases of mitral stenosis might also be expected to damp out the venous waves from the P.C.V.P. tracing. However, in Cases 4 and 5 the venous wave pattern was transmitted in full strength under just these conditions.

No immediate or delayed complications from the left atrial puncture were encountered, but two cases showed a considerable rise in P.C.V.P. as a result of inserting the bronchoscope. This emphasizes the potential danger of the procedure, which might well precipitate pulmonary œdema under certain conditions; fortunately this did not occur during the present study.

Summary

A method of recording immediately consecutive pressures in a blocked peripheral pulmonary artery (P.C.V.P.) and the left atrium in conscious patients with mitral valve disease is presented. Bronchoscopy was performed during cardiac catheterization and a needle introduced into the left atrium through the medial wall of the left main bronchus. The necessity for recording simultaneous or immediately consecutive pressures from the two sites is emphasized, because of their lability during bronchoscopy.

Seven patients suffering from mitral valve disease were selected to include examples of sinus rhythm, auricular fibrillation, low and high left atrial pressures, and low and high pulmonary arteriolar resistances. Mitral stenosis was present in five cases, mitral stenosis and incompetence in one, and pure mitral incompetence in the seventh.

In every instance the mean pressures in the left atrium and blocked peripheral pulmonary artery were found to be equal, and this confirms the view that the P.C.V.P. measured by cardiac catheterization is an accurate measurement of the left atrial pressure in mitral valve disease.

The P.C.V.P. tracing showed venous pulse waves similar in form to those recorded directly from the left atrium in every case, confirming the view that the true P.C.V.P. tracing should be venous in form and that the waves recorded are derived from the left atrium.

The authors wish to give grateful acknowledgment to Dr. Paul Wood for his encouragement during the investigation, and advice in the preparation of this paper. They also wish to express their appreciation for the technical assistance of Miss P. Scarlett, Miss D. Anderson, and Mr. J. Manders.

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PERSISTENT LEFT SUPERIOR VENA CAVA DRAINING THE PULMONARY VEINS

BY

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Persistence of the left superior vena cava is not uncommon in children with congenital heart disease and is occasionally found in adults at thoracotomy. The anomalous vena cava usually carries venous blood from the upper part of the body to the right atrium via the coronary sinus and has little functional significance. In the four patients we describe, however, the left superior vena cava drained arterial blood from some or all of the pulmonary veins into the left innominate vein, and thence into the right atrium. In three of them it was the sole channel by which oxygenated blood could reach the systemic circulation.

We record these cases because we believe that the anomaly is more common than has been thought, and gives a clinical picture sufficiently distinctive to be recognized in life, and because it is one for which surgical relief may prove feasible. We have found only two similar cases of which an account of the physical signs has been given and in neither was the diagnosis made in life (Taussig, 1947).

Before describing the clinical picture it is necessary to consider briefly the development of the superior vena cava.

EMBRYOLOGY

Marshall (1850), a century ago, appears to have been the first to give an embryological explanation of the persistence of a left superior vena cava.

A modern account of the anomaly (Hamilton *et al.*, 1945; Patten, 1946) is as follows. The venous system arises from the same network as the arterial system and the capillaries. Very soon three pairs of venous channels are recognizable, namely (i) the two vitelline veins, which pass from the yolk sac along the roof of the primative gut to meet (ii) the umbilical veins at the sinus venosus and (iii) the cardinal veins which also enter the sinus venosus. Each cardinal vein consists of two parts, the anterior cardinal or precardinal vein and the posterior cardinal or postcardinal vein. The precardinal and postcardinal veins unite on each side of the primative heart tube to form a short vessel, the common cardinal duct or duct of Cuvier which enters the horn of the sinus venosus (Fig. 1).

The lung bud arises as an outgrowth from the primitive foregut. Both these structures are covered by a common venous network, the splanchnic plexus. The contiguous primitive pulmonary venous plexus and primitive splanchnic venous plexus drain into the paired precardinal and postcardinal veins and into the vitello-umbilical veins (Fig. 3A). The paired precardinal veins of the embryo supply the venous drainage of the part of the body above the level of the sinus venosus. The postcardinal veins, by a complicated series of changes, give rise to the inferior vena cava and its tributaries. We are only concerned here with the precardinal veins.

Initially the precardinal veins are short, but they elongate as the neck develops and as the heart recedes into the thorax. During this time an obliquely directed transverse vein arises, which connects the two precardinal veins just caudal to the entrance of the veins of the forelimb. This transverse anastomosis forms the left innominate vein. The left precardinal vein, from the point where the left innominate vein leaves it to the left duct of Cuvier, normally becomes obliterated except for its most cephalad part which

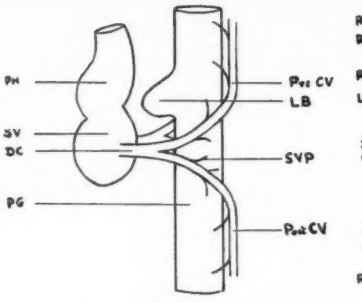


FIG. 1.—Diagram to show how the paired pre- and postcardinal veins receive blood from the venous plexus covering the primitive gut and lung bud, and deliver it by means of the duct of Cuvier into the sinus venosus. PH, primitive heart; SV, sinus venosus; DC, duct of Cuvier or common cardinal duct; Pre CV, precardinal vein; Post CV, postcardinal vein; PG, primitive gut; LB, lung bud; SVP, splanchnic venous plexus communications.

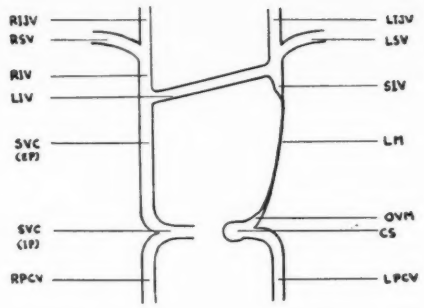


FIG. 2.—Diagram illustrating normal fate of the precardinal veins in man (see text for description). RIJV and LIJV, right and left internal jugular veins; RIV and LIV, right and left innominate veins; SVC(EP) and SVC(IP), superior vena cava, extra- and intrapericardial portions: RPCV and LPCV, right and left postcardinal veins; SIV, superior intercostal vein; LM, ligament of Marshall; OVM, oblique vein of Marshall; CS, coronary sinus.

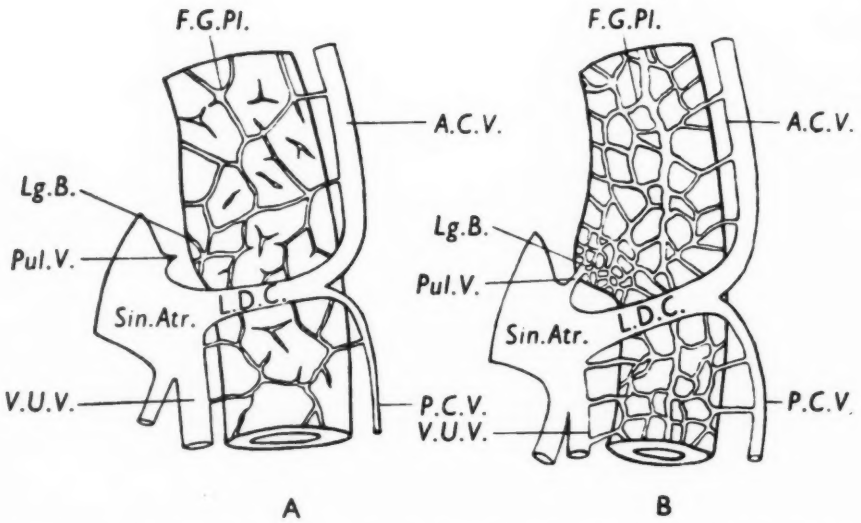


FIG. 3.—Diagram from H. Butler illustrating the formation and routes of drainage of the foregut venous plexus in the rat. (A) 3 *mm. rat embryo*. The foregut plexus (F.G.Pl.) drains into the cardinal and vitello-umbilical veins (V.U.V.). The cardiac part of the pulmonary vein has not yet "tapped" the foregut plexus. (B) 4·5–6 *mm. rat embryo*. The foregut plexus drains into cardinal, vitello-umbilical and pulmonary veins.

gives rise to the left superior intercostal vein (Fig. 2). The obliterated portion forms a fibrous band represented in the adult by the ligament of Marshall. The left duct of Cuvier and the left horn of the sinus venosus persist as the oblique vein of Marshall and the coronary sinus. That part of the right precardinal vein between the left innominate vein and the right duct of Cuvier forms the extrapericardial part of the superior vena cava, while the right duct of Cuvier forms its intrapericardial portion. The right horn of the sinus venosus is absorbed into the wall of the right atrium.

From the foregoing it will be seen that if the left precardinal vein is not obliterated it will persist as a left superior vena cava, receiving blood from the left innominate, internal jugular, and subclavian veins, and emptying into the right atrium at the coronary sinus. This is the commonest anomaly. The transverse anastomosis between the paired superior venæ cavæ may be absent and when this is so the venous drainage from each side of the upper part of the body is independent and the coronary sinus is large. At times the right superior vena cava is absent and the right innominate vein drains into the left superior vena cava.

Closely connected with persistence of the left superior vena cava are malformations of the venous return from the lungs. The stem of the pulmonary vein arises as an outgrowth from the dorsal wall of the sinus venosus (Butler, 1952) and, growing dorsally, forms the pulmonary part of the splanchnic venous plexus (Fig. 3B). Thereafter the pulmonary venous plexus drains directly into the heart and its communications with the cardinal and vitello-umbilical veins become obliterated. Failure of the cardiac part of the pulmonary vein to develop or to join the pulmonary venous plexus may result in persistent drainage of part or all of this plexus into the cardinal veins and thence either directly or indirectly into the right atrium.

Classification of Abnormalities

There are three ways by which the pulmonary veins can drain into the right atrium: they may open directly into its posterior wall; they may open into the coronary sinus; or they may drain into a persistent left superior vena cava and thence into the innominate vein, the right superior vena cava, and the right atrium. In any of these circumstances patency of the atrial septum is essential for life because it is the only way by which blood can reach the left heart.

McManus (1941) classified the various types of persistent left superior vena cava as follows.

I. Persistent left superior vena cava (*S.V.C.*) with right *S.V.C.* (bilateral *S.V.C.*).
   (A) Persistent left *S.V.C.* connected to the coronary sinus, and either with a cross anastomosis (left innominate vein) or without this.
   (B) Persistent left *S.V.C.* draining the pulmonary veins.

II. Persistent left *S.V.C.* without right *S.V.C.*

Our four cases are examples of Group I(B), namely persistent left superior vena cava draining the pulmonary veins.

Case Records

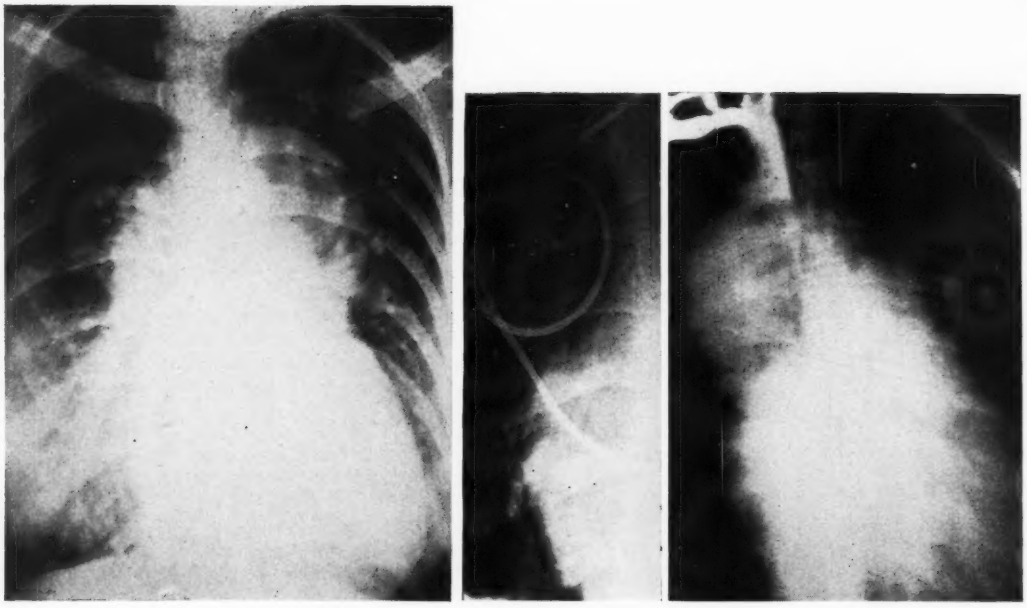
Case 1. M.M., a woman, aged 24, was admitted in January, 1949, complaining of dyspnœa on exertion. Breathlessness after feeds had first been noticed at the age of three months. She had attended a special school and had always been somewhat short of breath on walking uphill, though she could walk on the level without discomfort and had even played badminton. In July, 1948, she had become pregnant and at 22 weeks abdominal hysterotomy and sterilization had been performed.

On examination she was of small build (weight 93 lb.; height 5 ft., 1 in.). There was slight cyanosis and minimal finger clubbing. The pulse was 78 and regular; the blood pressure was 95/65 in the arms.

The left side of the chest was prominent and associated with considerable scoliosis. The apex beat was in the sixth intercostal space, 12·5 cm. from the mid-line and there was a forcible impulse over the outflow tract of the right ventricle and the pulmonary artery. The first sound at the apex was loud and widely split. A systolic murmur was audible over the whole præcordium, maximal in the second space near the left sternal border and louder in the upright position. An early diastolic murmur was heard in the third left space.

On fluoroscopy the right ventricle was considerably enlarged (Fig. 4A). The aortic knob was small. The pulmonary artery was prominent and its branches were large and showed expansile pulsation. There was a rounded pulsating shadow enveloping the great vessels in the superior mediastinum. A barium swallow was normal.

The electrocardiogram showed sinus rhythm, slight latent A-V block (P–R interval 0·22 sec.), and



A B C

FIG. 4.—Case 1. (A) Teleradiogram showing the rounded shadow of the venæ cavæ in the superior mediastinum enveloping the aortic knob and pulmonary trunk. (B) A–P film showing cardiac catheter coiled in the right superior vena cava. (C) Angiocardiogram, taken 2 sec. after the beginning of injection, showing the dilated right superior vena cava and simultaneous filling of the small aorta and large pulmonary trunk.

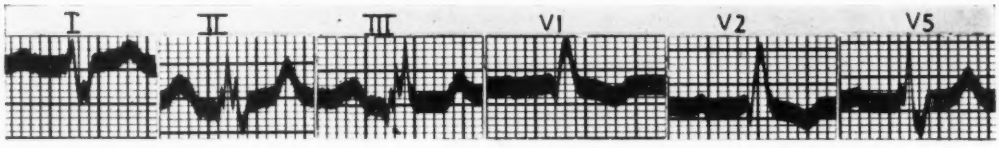


FIG. 5.—Case 1. Electrocardiogram showing sinus rhythm (P–R interval 0·22 sec.) and incomplete right bundle branch block.

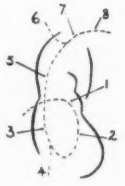
incomplete right bundle branch block (Fig. 5). Red blood corpuscles 5·5 million per cu. mm.; hæmoglobin 112 per cent.

The results of cardiac catheterization are summarized in Table I. The catheter coiled up in the greatly dilated right superior vena cava (Fig. 4B). The left atrium was reached without difficulty but the pulmonary veins could not be entered. The mean pressures in the right ventricle and pulmonary artery were a little high. The oxygen saturation of blood in the left innominate vein was 91 per cent and in the right internal jugular vein and the left subclavian vein it was 68 and 84 per cent respectively. The arterial blood oxygen saturation was 85 per cent.

The angiocardiogram taken 2 seconds after the injection of diodone showed dilatation of the right *S.V.C.* and simultaneous filling of the hypoplastic aorta and the large pulmonary arteries. The 5-second film showed diodone in the left *S.V.C.* and refilling of the right *S.V.C.*

In this patient it is thought that all the pulmonary veins drain into the left superior vena cava and that the systemic circulation is entirely dependent on the shunt through a patent foramen ovale or an atrial septal defect.

TABLE I. CASE 1, M.M., ÆT. 24



Sample of blood from:	O_2 content /100 c.c. bld.	O_2 capacity /100 c.c. bld.	Percentage sat'n.	Pressure mm. Hg. above skin of back
1. M.P.A.	16·1	17·2	93	24
2. R.V.			93	24
3. R.A.	—	—	79–87	13
L.A.	—	—	84	13
4. I.V.C.	12·0	—	70	—
5. S.V.C.	—	—	93	—
6. R.Int.Jug.V. ..	11·73	—	68	—
7. L.Innom.V.	—	—	91	—
8. L.Subclav.V. ..	14·4	—	84	—
Brachial artery ..	14·66	—	85	—

Pulmonary A-V oxygen difference (assuming P.V. 95% sat'd.)	=	3·3 ml./litre blood
Peripheral A-V oxygen difference	=	35·0 ml./litre blood
Pulmonary blood flow	=	48·5 litres/min.
Peripheral blood flow	=	4·6 litres/min.

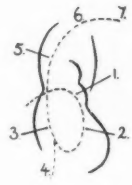
Case 2. R.T., a man, aged 24, was first seen in July, 1949. He had been short of breath all his life. He attended a special school till 14 and was unable to take part in games because of dyspnœa. He could walk only a few yards on the level and had been unable to work for the past eighteen months because of dyspnœa.

On examination he was a fit looking man with no cyanosis or finger clubbing. At rest there was no dyspnœa. The pulse was 84 and regular; the blood pressure in the arms was 120/80. There was recession of the intercostal spaces over the region of the apex beat and in the posterior axilla. The apex beat was palpable in the eighth left intercostal space in the mid-axilla some 17·5 cm. from the mid-line. The cardiac impulse was forcible and there was systolic expansion over the outflow tract of the right ventricle and the pulmonary artery. A moderately loud systolic murmur could be heard all over the præcordium and at the back and was maximal in the third left interspace near the sternum. The second sound in the pulmonary area was loud and widely split. A low pitched mitral diastolic murmur was audible at the apex.

On fluoroscopy the heart was displaced to the left and the right ventricle was greatly enlarged. The branches of the pulmonary artery were large and expansile pulsation was easily seen (Fig. 6). The vascular pedicle was wide forming an elliptical shadow within which the pulmonary artery and aortic knob could be seen. A barium swallow was normal. The cardiogram showed complete right bundle branch block (Fig. 7). Red blood corpuscles 5·7 million per cu. mm.; hæmoglobin 110 per cent.

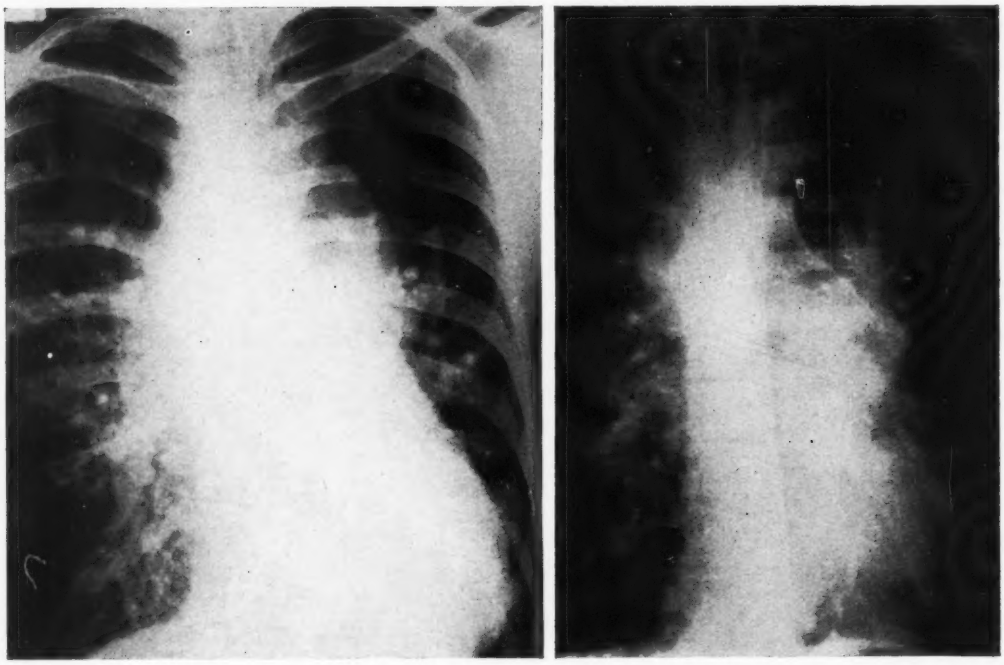
The results of cardiac catheterization are summarized in Table II. The catheter coiled up in the right *S.V.C.* as in Case 1; attempts to enter the left *S.V.C.* and the left atrium were unsuccessful.

TABLE II. CASE 2, R.T., ÆT. 24



Sample of blood from:	O_2 content /100 c.c. bld.	O_2 capacity /100 c.c. bld.	Percentage sat'n.	Pressure mm. Hg. above skin of back
1. M.P.A.	19·49	21·1	92	25
2. R.V.	—	—	95	26
3. R.A.	—	—	93–95	10
4. I.V.C.	19·01	—	90	—
5. S.V.C.	—	—	95	—
6. L.Innom.V.	—	—	95	—
7. L.Subclav.V. ..	17·92	—	85	—
Femoral artery ..	20·22	—	96	—

Pulmonary A-V oxygen difference (assuming P.V. 96% sat'd.)	=	7·3 ml./litre blood
Peripheral A-V oxygen difference	=	38·0 ml./litre blood
Pulmonary blood flow	=	34·0 litres/min.
Peripheral blood flow	=	6·6 litres/min.



A B

FIG. 6.—Case 2. (A) Teleradiogram showing the heart displaced to the left and large branches of the pulmonary arteries in the lung fields. The superior venæ cavæ form an elliptical shadow in the superior mediastinum enveloping the aortic knob and pulmonary trunk. (B) Angiocardiogram. Film taken 5 sec. after injection of diodone into right ventricle, showing the large vessel formed by the union of the right pulmonary veins passing to the left and then upwards into the left superior vena cava. The left pulmonary veins appear to enter the lower part of the left superior vena cava. The left innominate vein and the right *S.V.C.* also contain diodone.

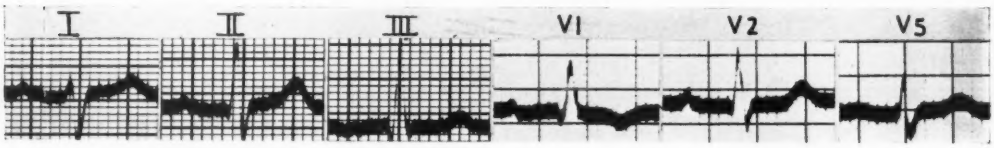


FIG. 7.—Case 2. Electrocardiogram showing complete right bundle branch block.

Mean pressures in the right ventricle and pulmonary artery were a little high. The oxygen saturation of blood in the left innominate vein was 95 per cent and in the left subclavian vein it was 85 per cent. The arterial blood oxygen saturation was 96 per cent.

The angiocardiogram taken 5 seconds after the injection of diodone by catheter into the right ventricle showed the right pulmonary veins uniting to form a single large vessel that ran transversely across the mid-line and turned upwards to be continued as the left *S.V.C.* The left pulmonary veins appeared to enter the latter at its lowermost part. Diodone could also be seen in the left innominate vein and the right *S.V.C.*

In this patient the fully oxygenated arterial blood and the failure to enter the left atrium at right heart catheterization were thought, in spite of the angiocardiographic evidence, to indicate

that some but not all of the pulmonary veins drained into the left *S.V.C.* and that the atrial septum was intact.

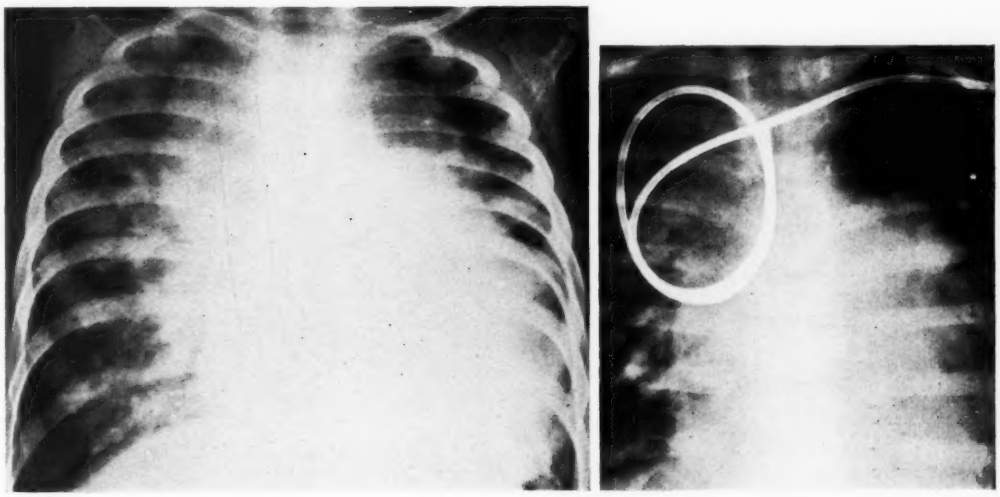
In view of the young man's considerable disability thoracotomy was advised in consultation with Sir Clement Price Thomas, with the object of anastomosing the left *S.V.C.* to the left atrial appendage. At operation it was found that a single large vein passed from the right lung transversely behind the heart towards the left hilum where it united with a similar single vein from the left lung to form the commencement of the left *S.V.C.* which thus drained all the pulmonary veins.

Unfortunately the left atrial appendage was abnormally small and for this reason its anastomosis to the *S.V.C.* proved technically impossible.

Case 3. C.B., an infant, aged 18/12, was physically and mentally backward; she was unable to sit up and could only just hold her head up. Nothing was known of her previous history except that she was the youngest of nine illegitimate children.

She was 26 in. long and weighed 14 lb. There was no finger clubbing but screaming induced slight cyanosis. The pulse was 138, regular, and of small volume; the blood pressure was 90/? in the arms. There was bulging of the præcordium and vigorous pulsation was visible and palpable all over the left side of the chest, particularly in the third and fourth spaces. The apex beat was in the fifth left space in the anterior axillary line. The second sound in the pulmonary area was loud and split. There was a loud harsh systolic murmur along the left sternal border, maximal in the third space, and a rumbling mitral diastolic murmur at the apex.

The teleradiogram showed that the heart was greatly enlarged and the main pulmonary artery and its branches were enormous (Fig. 8). There was an almost circular shadow in the superior mediastinum



A B

FIG. 8.—Case 3. (A) Teleradiogram showing the large heart and pulmonary trunk and enormous branches of the pulmonary artery in the lung fields. The shadows of the superior venæ cavæ envelop the pulmonary trunk and aortic knob. (B) A–P film showing cardiac catheter coiled in the right *S.V.C.*

within which, on the left side, the main pulmonary artery and what appeared to be the aortic knob could be seen. The cardiogram (Fig. 9) showed incomplete right bundle branch block with right ventricular enlargement. Hæmoglobin 77 per cent.

The results of cardiac catheterization are summarized in Table III. The left atrium was not entered. The mean pressures in the right ventricle and pulmonary arteries were extremely high. The oxygen saturation of blood in the left innominate vein was 94 per cent and in the left subclavian vein it was 66 per cent. The arterial blood oxygen saturation was 89 per cent.

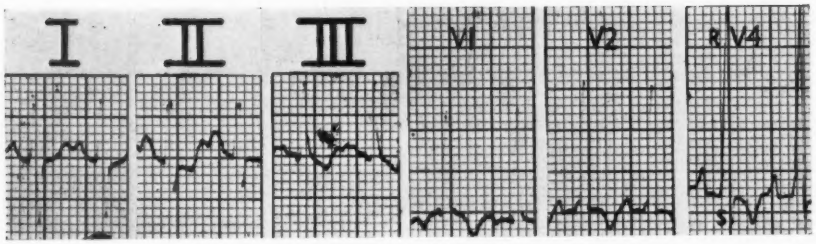
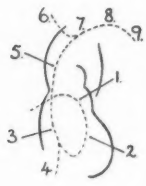


FIG. 9.—Case 3. Electrocardiogram showing incomplete right bundle branch block.

The angiocardiogram taken one second after injection of diodone by catheter into the right atrium showed an enormous right ventricle and simultaneous filling of the hypoplastic aorta and the large pulmonary artery (Fig. 10A). The 2-second film (Fig. 10B) showed diodone in both superior venæ cavæ and in the left innominate vein.

The child was anæsthetized for the angiocardiogram and immediately thereafter pulse and respiration were satisfactory. A few minutes later, however, she stopped breathing and no heart sounds could be heard. Restorative measures were unavailing and the child died.

TABLE III. CASE 3, C.B., ÆT. 18 MONTHS.



Sample of blood from:	O_2 content /100 c.c. bld.	O_2 capacity /100 c.c. bld.	Percentage sat'n.	Pressure mm. Hg. above skin of back
1. M.P.A.	14·02	15·9	88	70
2. R.V.	—	—	86	42
3. R.A.	—	—	87	10
4. I.V.C.	10·53	—	66	—
5. S.V.C.	—	—	92	—
6. R.Int.Jug.V. ..	—	—	55	—
7. L.Innom.V. ..	—	—	94	—
8. L.Subclav.V. ..	9·87 (Mean of 6, 8, 9)	—	66	—
9. L.Axillary V. ..	—	—	65	—
Femoral artery ..	14·17	—	89	—

Pulmonary A-V oxygen difference (assuming P.V. 95% sat'd.) = 10·8 ml./litre blood
Peripheral A-V oxygen difference = 39·7 ml./litre blood

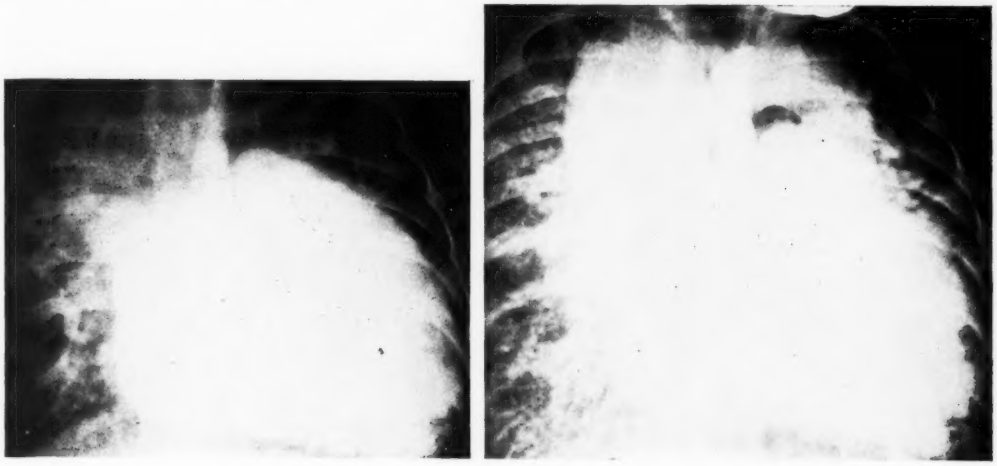
Post-Mortem Examination (Fig. 11 and 12). The right atrium was large. Its cavity measured 45 mm. from the right wall to the tip of the atrial appendage, and 28 mm. from the orifice of the *S.V.C.* to the tricuspid valve ring. The average thickness of the wall was 2 mm. The foramen ovale, 16 × 15 mm., was closed except for a narrow crescentic opening, 8 mm. in length at its anterior end.

The right ventricle formed the apex and nearly the whole of the anterior surface of the heart and was 55 mm. from base to apex. Its cavity measured 38 mm. from tricuspid ring to apex and 55 mm. from apex to the pulmonary valve ring. The wall of this ventricle was 6–8 mm. thick and the papillary muscles were hypertrophied, the larger measuring 6 × 4 mm. in cross-section. The tricuspid and pulmonary valves were normal.

The pulmonary trunk measured 22 mm. in diameter and its right and left branches were 15 mm. and 13 mm. wide, respectively. There was a dimple at the point of insertion of the obliterated ductus arteriosus.

The left atrium was small, 15 mm. from its summit to the mitral valve ring and 21 mm. from the interatrial septum to the root of the diminutive atrial appendage. Apart from the mitral ring, the only opening into this atrium was the crescentic aperture at the anterior end of the foramen ovale.

The left ventricle appeared as a small oval appendage applied to the left border of the right ventricle and was 38 mm. from base to apex. Its cavity measured 33 mm. from the mitral valve ring to the apex and its wall was only 4 mm. thick. The aorta was 9 mm. in diameter.



A B

FIG. 10.—Case 3. Angiocardiograms. (A) Film taken 1 sec. after injection of diodone into right atrium, showing enormous right ventricle and pulmonary trunk and the hypoplastic aorta. (B) Film taken 2 sec. after injection of diodone into right atrium, showing the heart and great vessels still filled with diodone and diodone in both superior venæ cavæ and the left innominate vein.

FIG. 11.—Case 3. Photograph of the heart and great vessels in situ, after removal of the anterior chest wall, showing the right ventricle (R.V.) occupying the whole anterior surface of the heart and the aorta (A) and pulmonary trunk (M.P.A.) enveloped above and on either side by the left innominate vein (C) and the right and left superior venæ cavæ (B, D respectively).

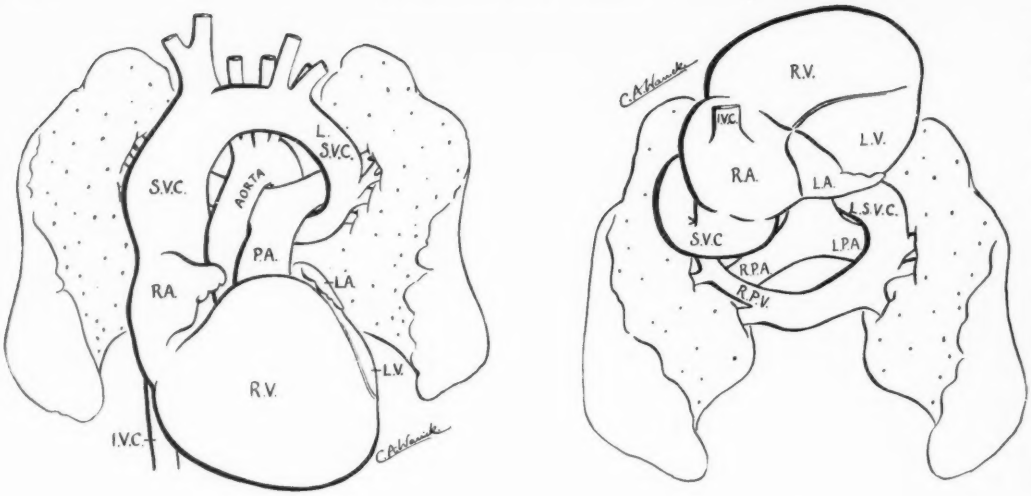


FIG. 12.—Case 3. Drawings of the heart and great vessels. (A) Viewed from the front. R.A., right atrium; I.V.C., inferior vena cava; R.V., right ventricle; P.A., pulmonary artery; L.A., left auricle; L.V., left ventricle; L.S.V.C., left superior vena cava; S.V.C. superior vena cava. (B) Viewed from the front with the heart lifted forwards, showing the pulmonary veins uniting to form the left superior vena cava. R.P.V., right pulmonary vein; R.P.A. and L.P.A., right and left pulmonary arteries.

The upper and lower right pulmonary veins (Fig. 12B) united to form a single large vessel, 12 mm. in diameter, which crossed transversely behind the heart towards the hilum of the left lung where it was joined by a large vein from the left lower lobe. Thereafter this vessel turned upwards and, having received the left upper pulmonary veins, became continuous with the left *S.V.C.* The cava was 18 mm. in diameter and at its upper extremity (Fig. 12A) it received the left subclavian and internal jugular veins and thereafter turned medially to become the left innominate vein which subsequently united with the right innominate to become the right *S.V.C.* The diameter of the latter in its widest part was 35 mm.

Thus, in this infant, all the pulmonary veins drained into the right atrium via the left *S.V.C.* and existence was maintained by what must have been a diminutive blood flow through the small crescentic opening in the foramen ovale.

Case 4. D.C., a boy, aged 13, was referred to hospital because on two occasions he had become cyanosed and severely dyspnœic after moderate exertion. He had always been small for his age but he led a normal life and took part in all the usual school activities.

In 1948 he was 50 in. high and he weighed 49 lb. There was no cyanosis or finger clubbing. The pulse was 80 and regular; the blood pressure was 110/70. The apex beat was in the fifth left space in the midclavicular line. There was a right ventricular type of cardiac impulse and palpable expansile pulsation over the outflow tract of the right ventricle and pulmonary artery. A third heart sound and a variable low-pitched mitral diastolic murmur were audible at the apex. The second sound in the pulmonary area was accentuated and widely split. A harsh, not very loud, systolic murmur was maximal in the second left space and audible over the whole præcordium and between the scapulæ.

On fluoroscopy (Fig. 13) the right ventricle was enlarged and there was increased pulsation in the pulmonary artery and its branches. There was a dilated right *S.V.C.* but no left *S.V.C.* was seen. Barium swallow was normal. The cardiogram showed incomplete right bundle branch block (Fig. 13). Hæmoglobin, 80 per cent.

The results of cardiac catheterization are summarized in Table IV. The left atrium was not entered. The mean pressures in the right ventricle and pulmonary artery were a little high. The

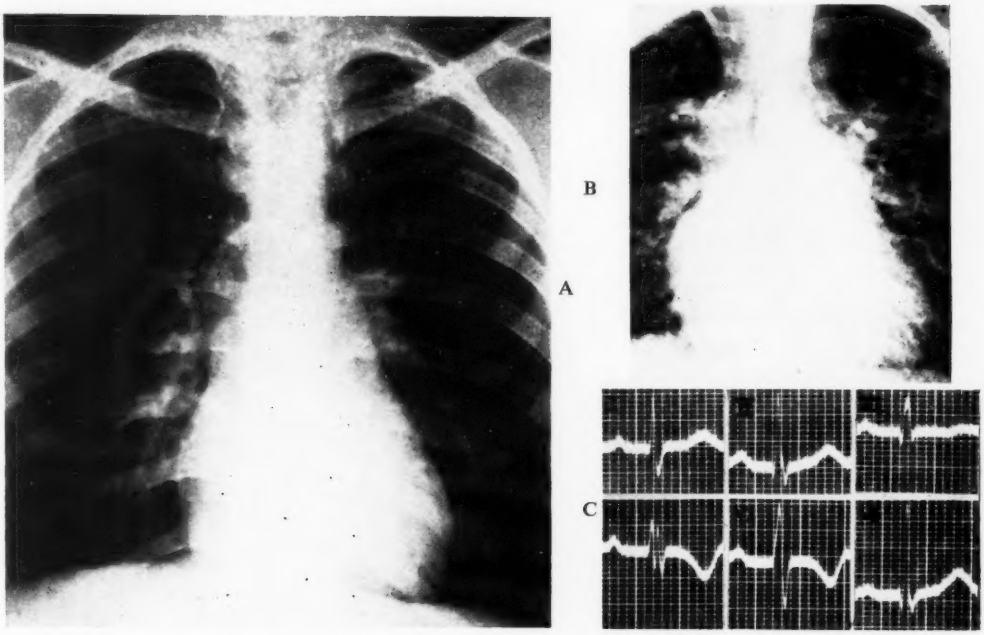
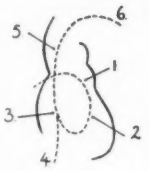


FIG. 13.—Case 4. (A) Teleradiogram showing the dilated right superior vena cava. (B) Angiocardiogram, taken 2 sec. after the beginning of injection, showing diodone in pulmonary artery and aorta. The left upper pulmonary vein passes upwards into the left superior vena cava and the left innominate vein contains diodone. The inferior pulmonary veins appear to drain into the left atrium. (C) Electrocardiogram showing incomplete right bundle branch block.

TABLE IV. CASE 4, D.C., ÆT. 13



Sample of blood from:	O_2 content /100 c.c. bld.	O_2 capacity /100 c.c. bld.	Percentage sat'n.	Pressure mm. Hg. above skin of back
1. M.P.A.	14·08	16·45	86	24
2. R.V.	—	—	84	21
3. R.A.	—	—	81–87	10
4. I.V.C.	12·63	—	77	—
5. S.V.C.	—	—	97	—
6. L.Subclav.V. ..	13·54	—	82	—
Femoral artery ..	15·9	—	97	—

Pulmonary A-V oxygen difference	=	18·2 ml./litre blood
Peripheral A-V oxygen difference	=	28·1 ml./litre blood
Pulmonary blood flow	=	9·9 litres/min.
Peripheral blood flow	=	6·4 litres/min.

oxygen saturation of blood in the right *S.V.C*, was 97 per cent, and in the left subclavian vein, 82 per cent. The arterial blood oxygen saturation was 97 per cent.

The angiocardiogram taken two seconds after the injection of diodone showed the left upper pulmonary vein passing upwards into a left *S.V.C.*, a large left innominate vein, and refilling of the large right *S.V.C.* Diodone was absent from the right atrium but present in the left, and the

inferior pulmonary veins from both sides appeared to drain into the latter chamber. The exact anatomy of the right upper pulmonary veins could not be determined with certainty but they were thought to drain into the right *S.V.C.*

In this child only the upper pulmonary veins have anomalous drainage and it is thought that the atrial septum is intact.

Clinical Picture

When the pulmonary veins drain into the left *S.V.C.* the clinical picture is characteristic and easily recognized in life. From an analysis of the physical signs in our four cases and of the two described by Taussig, the following clinical picture emerges.

The frequency of this particular anomaly it is difficult to assess. Earlier papers on this subject (McCotter, 1916; Papez, 1938) record some 200 examples of persistent left *S.V.C.* but do not distinguish the different types. It cannot be extremely rare, however, since we have encountered four examples in the past three years.

Symptoms and Signs. Surprisingly enough, this anomaly does not necessarily affect the general development although the left heart receives so little blood that it is commonly atrophic. Case 1 was a small asthenic woman, Case 2 was a large well-grown man, and Case 4, coincidentally, was a pituitary dwarf. Case 3 was mentally and physically defective, but it is impossible to say this was due to the cardiovascular abnormality.

The only important symptom is breathlessness on exertion, and this was noticed during the first year of life in our first two patients where all the pulmonary veins drained into the left *S.V.C.* In the fourth, where only the upper pulmonary veins had this anomalous drainage, dyspnœa was absent except for two attacks after severe exertion.

Cyanosis and finger clubbing may or may not be present and are never severe; both were slight in our first patient and absent in the other three.

The pulse volume tends to be small and the blood pressure somewhat low. Prominence of the left chest was obvious in our first three patients. All four had a well developed right ventricular type of impulse and in all there was expansile pulsation and a diastolic shock palpable over the pulmonary artery. The second pulmonary sound was accentuated and widely split in all four patients. Murmurs are not diagnostic. The only constant one is systolic and heard best to the left of the sternum; a basal diastolic and an apical mitral diastolic murmur may also occur.

The electrocardiogram showed complete or incomplete right bundle branch block in all four patients.

Radiology. The radiological appearance is characteristic. When all the pulmonary veins drain into the left *S.V.C.* there is a large ovoid shadow in the superior mediastinum, within which the aortic knob and the shadow of the pulmonary artery are clearly seen. This shadow is formed by the enormous right and left *S.V.C.* and the left innominate vein. Together with the heart shadow it gives an almost dumb-bell shaped silhouette.

When, as in Case 4, only some of the pulmonary veins have this anomalous drainage the appearances are far less striking but there is still considerable widening of the superior mediastinal shadow due to the dilatation of the right *S.V.C.*

The pulmonary arteries are large and show expansile pulsation. As would be expected the right ventricle is always enlarged.

Cardiac catheterization confirms the diagnosis. Blood samples from the left innominate vein and right *S.V.C.* are highly oxygenated and venous blood can be obtained only from the more peripheral veins.

Angiocardiography may demonstrate the abnormal course of the circulation and the right to left shunt through the atrial septal defect.

Prognosis. Brody (1942) states that the prognosis depends largely on the amount of blood diverted to the right atrium. In his series, of all the patients in whom the entire pulmonary drainage was into the right side of the heart, only three lived beyond early childhood. Taussig (1947)

considers the prognosis poor and states that death usually occurs between four and six months of age, although if the foramen ovale remains patent life may be prolonged for several years.

Our first two patients, both aged 24, are in reasonably good health though their activities are considerably restricted by dyspnœa, and in the first early congestive failure has been precipitated on one occasion by pregnancy. In our third patient existence, at the best, seemed precarious and it was thought that the mechanical interference only hastened the inevitably early fatal outcome. The fourth patient, aged thirteen years, leads a normal life.

The usual mode of death is said to be congestive failure and it is claimed, though the evidence is unconvincing, that this is brought about by the gradual closure of the defect in the atrial septum.

Differential Diagnosis. Atrial septal defect and large ventricular septal defects are the conditions most difficult to distinguish clinically from the variety of persistent left *S.V.C.* described here. Fluoroscopic examination, once the significance of the superior mediastinal shadow has been appreciated, makes the diagnosis obvious. Where doubt exists the finding of highly oxygenated blood in the left innominate vein will establish the diagnosis.

The fluoroscopic appearances may be confused with persistent azygos vein, aneurysmal dilatations of pulmonary artery or aorta, or in infants, an enlarged thymus gland. When there is a persistent azygos vein the shadow of the left *S.V.C.* is absent and catheter studies show that the abnormal vein contains venous blood. Aneurysmal dilatation of the pulmonary artery or aorta is easily excluded if the main pulmonary artery and the small aortic knob can be recognized within the shadow of the left *S.V.C.* An enlarged thymus may cause difficulty but it is usually possible to distinguish the lower poles of this organ, the so-called " sail-shadow," lateral to the cardiac silhouette.

Treatment. The only radical measure is an anastomosis of the left *S.V.C.* or the innominate vein to the left atrium or its appendage. This has never been done so far as we are aware. In our Case 2 the left atrium was found to be hypoplastic and could not be brought into apposition with either the left *S.V.C.* or the innominate vein. Brantigan (1947) has suggested that, provided it is certain that some of the pulmonary veins drain into the left atrium, the load on the right heart may be diminished by lobectomy and ligation of the anomalous veins.

Discussion

Failure of the left precardinal vein to become obliterated to form the ligament of Marshall results in persistence of the left *S.V.C.* This anomalous vessel may drain some or all of the pulmonary veins which therefore yield their blood to the right atrium instead of the left. If all the pulmonary veins empty into the right heart in this fashion a defect in the atrial septum is essential for life as it is the only pathway by which blood can reach the left side of the heart.

The most striking signs of this anomaly indicate the large left to right shunt, and in this respect resemble those of atrial septal defect and large ventricular septal defects, only they are exaggerated. The right to left shunt, which must be present when all the pulmonary veins drain into the right atrium, may be impossible to detect clinically since the presence or absence of cyanosis depends on the oxygen saturation of blood in the right atrium from which the left heart is entirely supplied, and in our patients this ranged from 79 to 95 per cent.

This highly oxygenated right atrial blood suggests that the pulmonary flow is many times greater than the systemic. That the pulmonary flow is large is evident from the considerable expansile pulsation, palpable over the right ventricle and pulmonary artery and visible fluoroscopically in the branches of the pulmonary artery in the lung fields. The load on the right heart must be extremely heavy because it receives almost the entire systemic and pulmonary venous blood. This results in very great hypertrophy of the right ventricle which is recognized clinically by the forceful right ventricular thrust, the loud and widely split pulmonary second sound, partial or complete right bundle branch block, and the radiological appearances. The small pulse volume and low blood pressure is evidence that the systemic flow is small, and the atrophic left atrium

and ventricle and hypoplastic aorta found at autopsy likewise suggest that the left heart receives very little blood.

The catheter findings provide some idea of the order of the discrepancy between pulmonary and peripheral flows. The figures can only be regarded as very rough approximations, however, because in no case was it possible to sample blood from the pulmonary veins, and it was quite impossible to obtain an accurate figure for the oxygen content of systemic venous blood.

The severe pulmonary hypertension present in our third case may be compared with the findings in atrial septal defect, where in the majority of patients the mean pressure in the pulmonary artery is within normal limits but in a small minority there is pulmonary hypertension sufficient, on occasion, to result in tricuspid incompetence and partial reversal of the inter-atrial shunt. The poor physical state of this infant suggests that the prognosis may be adversely affected by the presence of much pulmonary hypertension.

The diagnostic value of right heart catheterization in this condition is unquestionable, since in no other anomaly is arterial blood found in the left innominate vein. By contrast angiocardiography is far less useful because the immense pulmonary flow quickly dilutes the contrast media, even if it be introduced directly into the right ventricle, and in consequence the abnormal anatomy of the venous side of the pulmonary circulation is poorly defined.

The obvious radical therapeutic measure is anastomosis of the left *S.V.C.* to the left atrium or its appendage, but our experience, gleaned from one exploratory thoracotomy and one autopsy together with the evidence from anatomical descriptions (Papez, 1938), suggests that these structures may not uncommonly be atresic so that surgical correction of the anomaly may rarely be feasible.

Summary

The development of the superior vena cava and pulmonary veins is outlined and the types of persistent left superior vena cava are classified.

Four cases of a persistent left superior vena cava draining pulmonary veins are reported. In one the diagnosis was confirmed at operation, and in a second at autopsy.

The clinical picture is described. The essential features are evidence of an enormous left to right shunt, considerable right ventricular enlargement, little or no cyanosis, and fluoroscopically the wide mediastinal shadow enveloping the aortic knob and pulmonary arc. The diagnosis is confirmed by cardiac catheterization when arterial blood is found in the left innominate vein.

The differential diagnosis is discussed. The condition is not rare, does not necessarily lead to death in infancy or childhood, and can be diagnosed during life. Surgical correction of the anomaly was attempted in one patient but was impracticable. The scope of surgical measures is briefly considered.

It is a pleasure to record our thanks to Dr. Clifford Hoyle for his help and advice in the preparation of this paper and for allowing us to study one of his patients (Case 1). We are also indebted to Dr. B. Gans, who kindly referred Case 3 to us, and to Dr. Ann Warwick and the Photographic Department of the Royal Free Hospital for the illustrations.

Since this paper was completed we have seen a report on this subject by Snellen and Albers (*Circulation*, Dec., 1952). Their findings and conclusions agree closely with our own.

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THE ANGIOCARDIOGRAM IN FALLOT'S TETRALOGY

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While the principal angiocardiographic features of the tetralogy of Fallot have been listed by many authors, the number of cases described in detail or illustrated is relatively small. Recently Dotter and Steinberg (1951) reviewing the subject emphasized the need for further observations with necropsy control in cyanotic congenital heart disease.

A final clinical diagnosis of Fallot's tetralogy was made in nearly one-third of the first 160 patients investigated by angiocardiography at the National Heart Hospital and at the Brompton Hospital. The results in this group have been analysed, and the appearances correlated with such surgical and post-mortem findings as were available.

Technique. Although slightly modified, the technique employed was essentially that described by Robb and Steinberg (1939). Diodone was injected through a wide-bore plastic cannula introduced into the median cubital vein. Venous pooling of contrast material was reduced by advancing the cannula tip to the subclavian vein; and by injecting, immediately after the diodone, 10 to 15 ml. of saline previously layered above it in the syringe. Since 1948 when Dr. M. McGregor devised a perforated plastic disc for introduction between diodone and saline during the loading of the syringe, this method of preventing mixing before the injection has been routinely employed. The injection of one ml. of 70 per cent diodone per kg. body weight usually took less than two seconds.

The hand-operated multiple-cassette changer at the Brompton Hospital was constructed by McGregor (1949), and that used at the National Heart Hospital was a modified copy of this machine. The patient was recumbent, and with either apparatus it was possible to expose nine films in six seconds. Anode-film distance was 48 inches.

With few exceptions the investigation was performed under thiopentone anæsthesia.

Material and Method

Fifty patients with Fallot's tetralogy were investigated. The diagnosis was supported in twenty-nine by the results of cardiac catheterization, and in thirty-one by the findings at operation, which included a direct attack on the site of stenosis in fifteen. In six cases necropsy confirmation was eventually obtained. At the time of this study there remained six cases where the diagnosis rested entirely on clinical and angiocardiographic evidence; but in none of these was there any reasonable doubt as to the nature of the malformation.

The following analysis refers, except where otherwise indicated, to the appearances in the antero-posterior view. Films in this projection were available in 47 cases, while oblique or lateral angiocardiograms were taken in 12 only.

The interpretations were subject to certain limitations. The relatively slow operating speed of the cassette changers introduced a possible error of approximately 0·7 sec. in the timing of events. No attempt was made to measure the size of the right ventricle or infundibulum, for the exact phase of the cardiac cycle at which a film had been exposed was not known. It was necessary to assess the size of the pulmonary arteries in an arbitrary fashion as large or normal or small, because normal standards for the calibre of these vessels have not been established under comparable conditions;

though measurements made from angiocardiograms taken at an anode-film distance of 72 inches have been published (Dotter and Steinberg, 1949).

The Appearances in Fallot's Tetralogy

While films that demonstrate both a right to left shunt and pulmonary stenosis are not necessarily diagnostic of Fallot's tetralogy, these are the basic angiocardiographic appearances of the malformation.

The Shunt. In most cases a right to left shunt was shown by early opacification of the proximal thoracic aorta. Occasionally premature aortic filling was not convincingly demonstrated and the only certain evidence of the small shunt was faint opacification of a subclavian artery (Fig. 1), a sign emphasized by Campbell and Hills (1950). In these circumstances filling of the systemic vessel

Fig. 1.—Fallot's tetralogy. Stenosis believed to be valvular at Blalock-Taussig operation. Angiocardiogram at 2 seconds showing pulmonary arterial enlargement. There is some opacification of the left subclavian artery.

Fig. 2.—Fallot's tetralogy. Stenosis believed to be subvalvular at Blalock-Taussig operation. Angiocardiogram at 2 seconds. An infundibular chamber is shown. The aortic arch is right-sided.

might not be visible until the second film to show diodone in the pulmonary artery; but in all other cases both the aorta and the pulmonary artery were first visualized in the same film.

It is widely recognized that premature opacification of the left ventricle may occur in Fallot's tetralogy (Sussman and Grishman, 1947; Ulfsparre, 1949; Dotter and Steinberg, 1951); but this was seen in fewer than half the cases in the present series. When visible, early left ventricular opacification was usually faint, but it was of moderate density in four cases, one of which is illustrated in Fig. 3.

The Stenosis. The site of stenosis was seldom directly visualized, but the demonstration of an infundibular chamber (Fig. 2) sometimes provided conclusive though indirect evidence of stenosis. With the technique employed, however, it is unusual for the infundibulum to be well filled, not only in Fallot's tetralogy (Cooley *et al.*, 1949), but also in normal subjects (Dotter and Steinberg, 1949); and, as Thompson *et al.* (1949) emphasized, a single film may give a false impression of infundibular narrowing. On the other hand visualization of an apparently normal right ventricular outflow tract and pulmonary valve area does not exclude pulmonary stenosis (Dotter and Steinberg, 1951). Features that might indirectly indicate pulmonary stenosis were therefore sought. Attention was

directed to the size of the pulmonary arteries and to the time of onset and the density and duration of opacification of these vessels.

Reduction in calibre of the pulmonary arterial tree sometimes suggested the presence of stenosis (Fig. 3); but not infrequently the major arteries were normal in size or even enlarged (Fig. 1), and often no convincing abnormality of the lung vascular pattern could be detected. Campbell and Hills (1950) found that pulmonary stenosis did not delay filling of the pulmonary arteries, and this was confirmed; in no case was opacification of these vessels shown to occur later than that of the aorta. Moreover, in spite of the stenosis the pulmonary arteries were usually densely opacified. Delayed emptying of the pulmonary vessels has been noted in the presence of pulmonary stenosis (Ulfsparre, 1949; Campbell and Hills, 1950; Cooley, 1951). In the present series the duration of opacification of the major pulmonary arteries tended to be greater in both Fallot's tetralogy and pulmonary stenosis with intact ventricular septum than in control subjects (Fig. 4). The overlapping of the groups may be partly due to the younger ages of those with pulmonary stenosis, for the circulation of diodone is normally more rapid in children than in adults (Steinberg *et al.*, 1943). Undue persistence of diodone in the lung vessels may, however, also occur in mitral stenosis (Angelino and Actis Dato, 1952), in the Eisenmenger complex (Campbell and Hills, 1950; Cooley, 1951; Soulié *et al.*, 1951*b*), and in other conditions associated with a severe pulmonary hypertension (Fig. 4).

FIG. 3.—Fallot's tetralogy. Angiocardiogram at 2½ seconds. The pulmonary arteries are small but well opacified. There is considerable early filling of the left ventricle.

OTHER FINDINGS OF ANATOMICAL OR PHYSIOLOGICAL SIGNIFICANCE

Right Ventricular Hypertrophy. Hypertrophy of the right ventricle was included by Carson *et al.* (1948) and by others who have listed the angiocardiographic findings in Fallot's tetralogy. In the present series evidence for this in antero-posterior films was unconvincing. In such lateral or oblique angiocardiograms as were available the interventricular septum was sometimes convex to the left, a sign of right ventricular hypertrophy put forward by Sussman *et al.* (1942); but it was not always possible to distinguish this border from the posterior margin of the right atrium.

Dextroposition of the Aorta. Usually the position of the base of the aorta in antero-posterior films gave no real indication of the presence, let alone the degree, of anatomical aortic override. The density of early aortic opacification was not accepted as evidence of the anatomical relations of the aortic orifice; it merely reflected the size of the shunt under angiocardiographic conditions.

Vascular Abnormalities. There was a right-sided aortic arch in six patients, but the other anomalies of the great vessels found in coincidental association with the tetralogy of Fallot will not be enumerated. Those involving the aorta and its branches caused no difficulty in interpretation. The significance of apparent malformations of the major pulmonary arteries was less readily determined. Cooley *et al.* (1949) pointed out that failure to demonstrate one of these by angiocardiography does not disprove its existence. In one case the films strongly suggested, and necropsy later confirmed, absence of the left pulmonary artery; the right pulmonary artery passed posteriorly before turning to cross the mid-line, and in the lateral view this was responsible for a shadow

suggesting a blind diverticulum at the site of origin of the left pulmonary artery (Fig. 5): bronchial arteries supplied the left lung but were not visible in the angiocardiogram.

Large bronchial arteries arising from the aorta were seen only in patients believed to have pulmonary atresia and therefore excluded from this discussion; but in some cases of Fallot's tetralogy the lung vascular pattern showed features indicative of an increased bronchial blood supply (Campbell and Gardner, 1950). Occasionally the internal mammary arteries were prominent, and in one case large tortuous intercostal arteries on the left side were associated with slight unilateral rib notching (Fig. 6). At the age of ten this thirty-year-old patient had had a respiratory infection in the course of which fluid was removed from the left pleural cavity; he maintained that during the succeeding months his cyanosis had lessened and his exercise tolerance had improved considerably.

The Site of the Stenosis. The development of intra-cardiac surgery (Brock, 1948; Brock and Campbell, 1950) as an alternative to the anastomotic operation (Blalock and Taussig, 1945) has

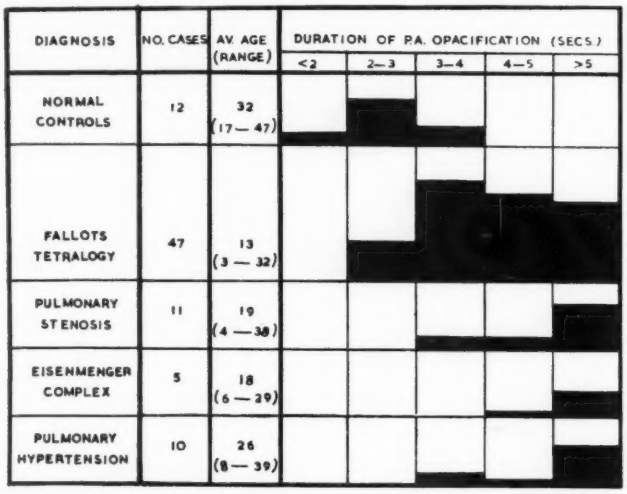

FIG. 4.—Duration of opacification of left or right pulmonary artery, whichever was the more readily visible, in (1) normal controls, (2) Fallot's tetralogy, (3) pulmonary stenosis with intact ventricular septum, (4) Eisenmenger's complex, and (5) severe pulmonary hypertension. In some cases of group (5) this was associated with patent ductus arteriosus through which flow was reversed; in others a ventricular septal defect was suspected but not proven. In both pulmonary stenosis and pulmonary hypertension, whether the ventricular septum was defective or intact, opacification of the pulmonary arteries tended to persist for longer than in normal subjects.

made the precise determination of the site of stenosis in Fallot's tetralogy a matter of some importance. Selective angiocardiography (Jönsson *et al.*, 1949; Soulié *et al.*, 1951*b*) would seem to be the most effective technique for revealing the detailed anatomy of the obstruction, but it was of interest to discover how much information could be obtained from intravenous angiocardiograms. Of the 18 cases where the level of stenosis was determined at direct operation or at necropsy, it was valvular in 8 and subvalvular in 9: in the remaining one necropsy revealed a high infundibular obstruction, with a small infundibular chamber, and also a tight valvular stenosis.

In three cases with proven subvalvular stenosis there was clear evidence of the level of stenosis. In two (Fig. 5 and 7) an infundibular chamber was demonstrated, and in the third there was an

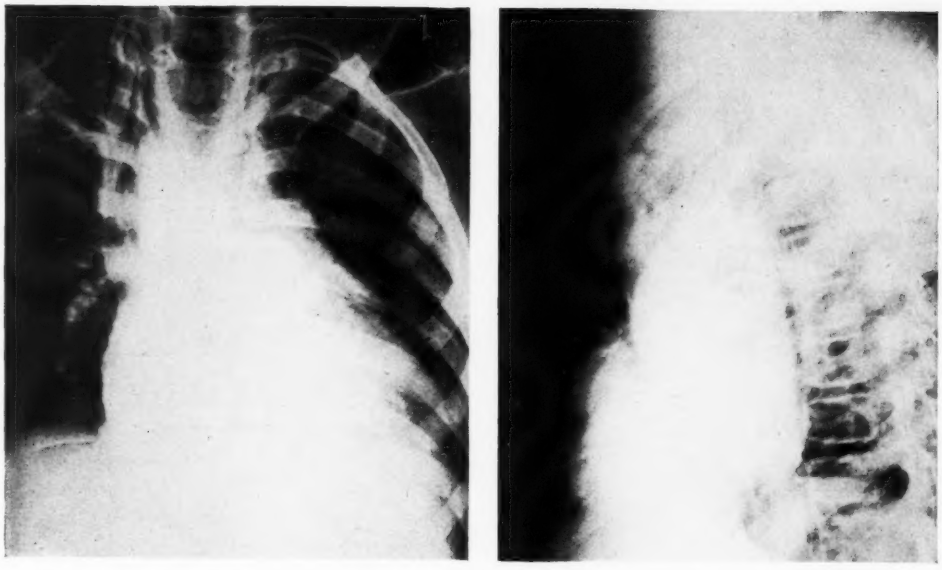

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FIG. 5.—Fallot's tetralogy with subvalvular stenosis, an infundibular chamber, and absence of left pulmonary artery (necropsy). (A) Antero-posterior angiocardiogram at 2 seconds, showing infundibular chamber and right-sided aortic arch. No left pulmonary artery is visible. (B) Left lateral angiocardiogram at 3 seconds. The opacity at the expected site of origin of the left pulmonary artery is the right pulmonary artery.

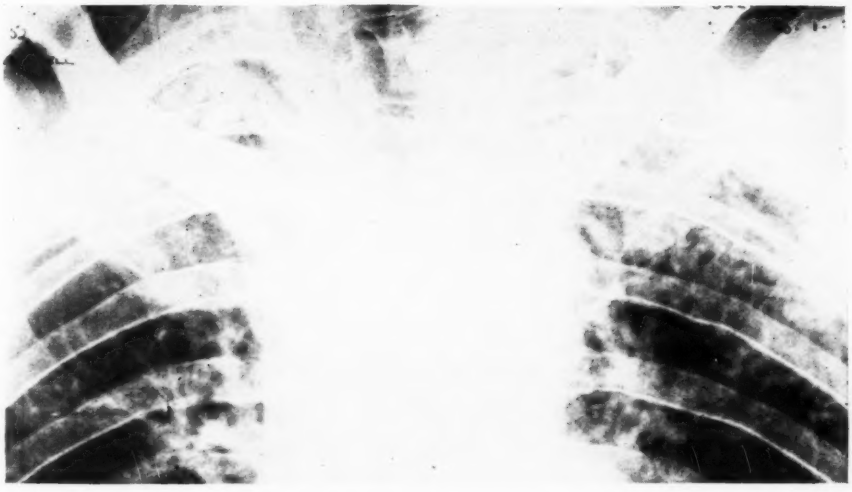

FIG. 6.—Fallot's tetralogy. Part of angiocardiogram at 4 seconds, showing on the left side, enlarged intercostal arteries, and slight rib notching (see text).

abrupt narrowing of the right ventricular outflow tract. In all three these appearances persisted essentially unchanged in three or more consecutive films. When this tract was not well opacified, care was necessary to avoid mistaking the shadows cast by the descending branches of the left pulmonary artery for diodone in the infundibulum; but in several cases of subvalvular stenosis a persistent though faintly outlined infundibular deformity was visible although the degree of narrowing could not be estimated. A similar appearance was noted in two patients with valvular stenosis, and Soulié *et al.* (1951, *a* and *b*) have emphasized that narrowing and irregularity of the infundibulum is usual in Fallot's tetralogy regardless of the site of maximal obstruction. However, in two

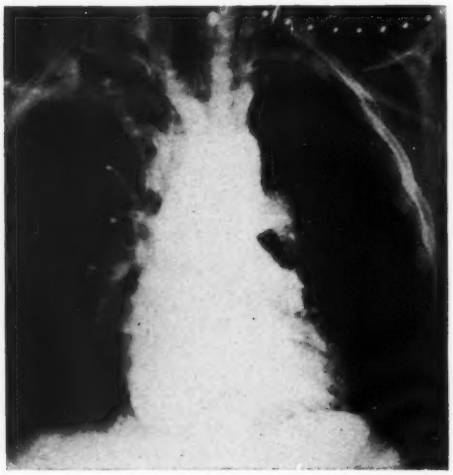

FIG. 7.—Fallot's tetralogy with valvular as well as infundibular stenosis (necropsy). Angiocardiogram at 2½ seconds showing the infundibular chamber. The left pulmonary artery is relatively large and the appearances suggest fusiform dilatation of this vessel.

FIG. 8.—Fallot's tetralogy with valvular stenosis (necropsy). Angiocardiogram at 2 seconds. The right ventricular outflow tract is medially situated (compare Fig. 5 and 7).

patients with valvular stenosis the right ventricular outflow tract was well opacified and apparently undeformed, an appearance not seen in any proven case of infundibular stenosis.

In subvalvular stenosis, when the right ventricular outflow tract was visualized it was displaced to the left, and the infundibulum and pulmonary trunk were approximately parallel to the left heart border (Fig. 5 and 7). Brock and Campbell (1950) noted the almost horizontal course sometimes taken by the infundibulum in subvalvular stenosis. In valvular stenosis, on the other hand, the right ventricular outflow tract was usually more medially situated and almost vertical, commonly being superimposed on the left border of the spine or on the descending aorta (Fig. 8).

A persistent filling defect, with an upward convexity or peak at valve level, is sometimes found in pulmonary valvular stenosis with a closed ventricular septum (Fig. 9). This appearance was not seen in any patient with Fallot's tetralogy where the site of stenosis had been proven, though it was visible in two cases in the series.

In general the pulmonary trunk was larger in valvular than in subvalvular stenosis, but there were exceptions. Loss of parallelism of the walls of this vessel was more frequently observed and was usually greater in valvular than in subvalvular stenosis; but in two cases of valvular stenosis where the main pulmonary artery was clearly defined no fusiform dilatation could be detected.

The left pulmonary artery tended to be more prominent when the stenosis was valvular, but it was not always small in infundibular stenosis. It is possible that the shape of this vessel is of greater significance than its calibre. In some patients with valvular stenosis the antero-posterior angiocardiogram suggested that fusiform dilatation of the pulmonary trunk was maximal not proximally but distally, and that it spread beyond the bifurcation to involve the first part of the left pulmonary artery. Certainly this may occur in valvular pulmonary stenosis with intact ventricular septum (Fig. 13); and fusiform dilatation of the left pulmonary artery sometimes makes a significant contribution to the prominence of the pulmonary arc characteristically shown by conventional radiology in these cases. Although in all other respects the angiocardiogram of Fallot's tetralogy illustrated in Fig. 7 points to subvalvular obstruction, there appears to be fusiform dilatation of the left pulmonary artery, and possibly this should have suggested that valvular stenosis was also present.

FIG. 9.—Pulmonary stenosis with intact ventricular septum and inter-atrial communication (necropsy). Angiocardiogram at 3½ seconds. The ventricle and the aorta are well filled and the stenosed valve is outlined. Left atrial opacification was not visible now or earlier in this view.

Of the 18 angiocardiograms under discussion the site of stenosis was clearly demonstrated in three, and suggested by indirect evidence in eight. No real indication of the level of obstruction was given in the remaining seven but the quality of the films was below average in four of these. In ten other cases the probable site of stenosis was determined by direct examination of the heart as described by Brock (1948); but, because an anastomotic operation was performed, conclusive proof is lacking. Of these the level of stenosis was clearly shown by the angiocardiogram in three cases and indirectly indicated in four; in one the surgeon concluded that the obstruction was valvular but the films suggested that it was infundibular; and in the remaining two the angiocardiograms gave no evidence of the site of stenosis.

Physiological. Although in general the most dense early aortic opacification, the smallest pulmonary arteries, and the most lengthy persistence of diodone in the lung vessels were seen in the most disabled patients, the quantitative angiocardiographic estimates of right to left shunting and of pulmonary blood flow added little to the clinical assessment. However, reopacification in late films of the left heart and aorta by contrast material that had passed through the pulmonary circulation sometimes gave confirmatory evidence of relatively good pulmonary flow. This appeared earliest and was most dense in those patients where the pulmonary flow was believed on clinical and other grounds to be least reduced.

DIFFERENTIAL DIAGNOSIS

The angiocardiogram of itself was rarely diagnostic of Fallot's tetralogy, and usually the most that could be claimed was that the appearances were compatible with the clinical diagnosis. Nonetheless the investigation was of value in differentiating the tetralogy from other malformations; and, although an exhaustive account of angiocardiographic differential diagnosis is not justified by the study of so small a series, two conditions in which the angiocardiogram may be similar to that of Fallot's tetralogy will be briefly considered.

FIG. 10.—Pulmonary stenosis and inter-atrial communication; ventricular septum probably intact (valvotomy). Angiocardiogram at 2 seconds showing premature opacification of the left atrium.

FIG. 11.—Pulmonary stenosis with intact ventricular septum and inter-atrial communication (valvotomy). Same patient as Fig. 13. Left lateral angiocardiogram at 1½ seconds. Premature opacification of the left atrium is clearly shown.

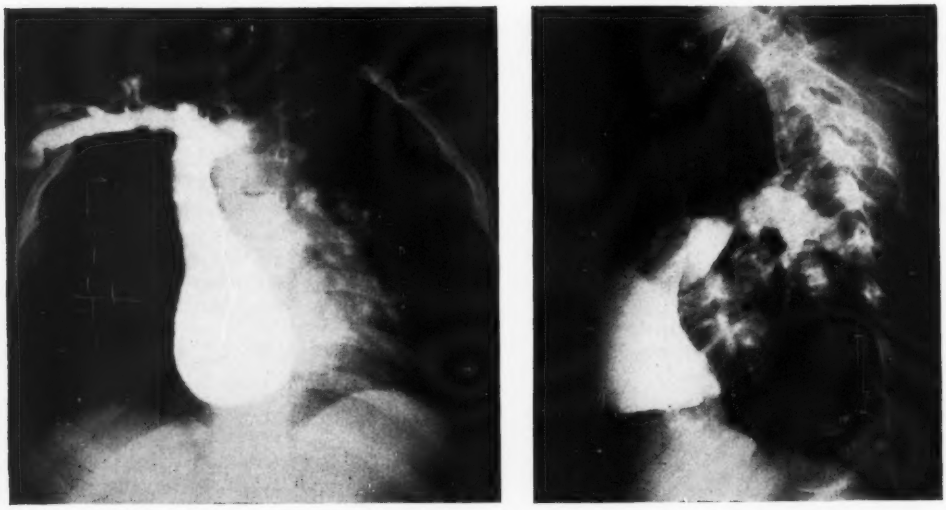

FIG. 12.—Fallot's tetralogy. (A) Antero-posterior angiocardiogram at 1½ seconds. Opacification of a large and unusually medial right atrial appendage resembles premature filling of the left atrium. (B) Left lateral angiocardiogram at 1½ seconds. The right heart is well opacified but diodone has not passed to the left atrium.

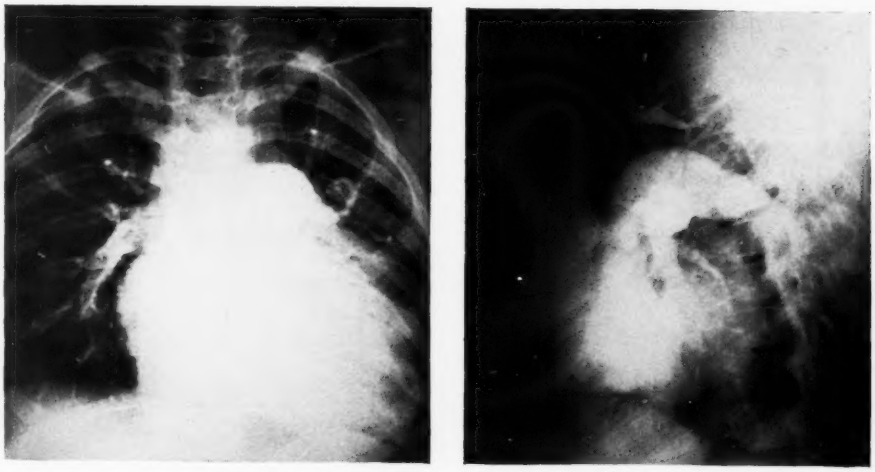

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FIG. 13.—Pulmonary stenosis with intact ventricular septum and inter-atrial communication (valvotomy). (A) A–P angiocardiogram at 4½ seconds showing pulmonary arterial enlargement. (B) Left oblique angiocardiogram at 3 seconds. The dilatation of the pulmonary trunk is maximal distally and extends into the left pulmonary artery.

The Eisenmenger Complex. Premature aortic opacification was visible in the angiocardiograms of five cyanosed patients with pulmonary hypertension and ventricular septal defect, the appearances closely resembling those in Fallot's tetralogy where the area of stenosis was not visible. Even when an apparently normal infundibulum and pulmonary valve region were demonstrated pulmonary stenosis could not be excluded (Dotter and Steinberg, 1951).

In no case of the Eisenmenger complex were the major pulmonary arteries reduced in size; but in one only was there gross pulmonary arterial dilatation, and the slight or moderate enlargement present in the other four was no greater than that sometimes seen in Fallot's tetralogy (Fig. 1). Rounded opacities in the lung fields, representing enlarged pulmonary artery branches in cross-section, were visible in four angiocardiograms of the Eisenmenger complex, but a not dissimilar appearance was occasionally noted in Fallot's tetralogy. De Groot (1951) claimed that contrast material reached the left atrium more quickly in the Eisenmenger complex than in Fallot's tetralogy, but no such difference was found in this series, diodone tending to be held up in the pulmonary arteries in both conditions (Fig. 4).

Miller (1950) stressed the difficulty of distinguishing between the Eisenmenger complex and Fallot's tetralogy by means of angiocardiography, and although the films usually show features that favour one or the other malformation, it is agreed that this differential diagnosis can be made with greater assurance in other ways.

Pulmonary Stenosis with Intact Ventricular Septum. Angiocardiograms of six patients with pulmonary stenosis and intact ventricular septum, where cyanosis was due to an inter-atrial shunt, were compared with those of Fallot's tetralogy. The diagnosis was eventually confirmed at necropsy in three; and in the other three, later subjected to valvotomy, the clinical impression was supported by the results of cardiac catheterization. These films resembled those of the tetralogy in so far as there was premature aortic opacification in all cases, and definite evidence of pulmonary stenosis in some. In pulmonary stenosis with intact ventricular septum, as in the tetralogy, filling of the aorta and of the pulmonary artery usually first appeared in the same film; moreover, the density of

aortic opacification in severely cyanosed patients (Fig. 9 and 14) was comparable to that seen in many cases of Fallot's tetralogy.

Early filling of the left atrium (Fig. 10) is the key to the angiocardiographic differentiation between these malformations, but in the antero-posterior view this was occasionally simulated by opacification of the right atrial appendage (Fig. 12). Again, films in this projection sometimes failed to demonstrate premature filling of the left atrium, even though considerable central cyanosis indicated that the inter-atrial shunt was large (Fig. 9 and 14). In these it seemed that left atrial opacification was fleeting and that, because the ascending aorta was already filled in the first film to show contrast material beyond the right atrium, any residual traces of diodone remaining in the left atrium at this time were concealed by the aortic shadow.

When early left atrial filling was doubtful in the antero-posterior view left lateral films were decisive on this point (Fig. 11); but twice at least uncertainty as to the diagnosis remained. In these cases, although early left atrial opacification was shown in the lateral projection, it was faint and transient and seemed inadequate to account for the denser and more persistent filling of the aorta. In both patients this apparent discrepancy appeared to favour Fallot's tetralogy with patent foramen ovale, through which a small right to left shunt had occurred under angiocardiographic conditions. Both died after valvotomy and in both necropsy revealed pulmonary stenosis with a large inter-atrial communication and without ventricular septal defect. When the angiocardiograms (Fig. 9 and 14) were reviewed it was noted that early left ventricular opacification was more complete and greater in density than was commonly seen in Fallot's tetralogy. While dense early left ventricular filling may occasionally occur in Fallot's tetralogy (Fig. 2), it is certainly exceptional when the injection is made intravenously, and should at least arouse suspicion of an alternative diagnosis (Donzelot *et al.*, 1949).

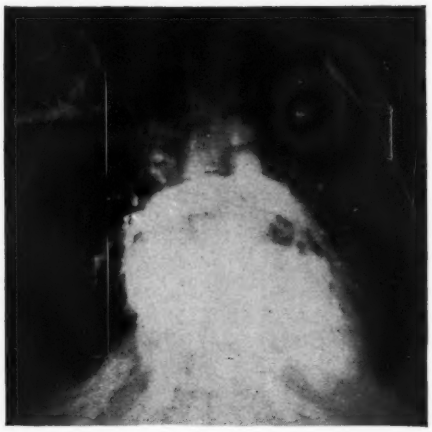

FIG. 14.—Pulmonary stenosis with intact ventricular septum and inter-atrial communication (necropsy). Angiocardiogram at 1½ seconds. The left ventricle and aorta are already visualized, but filling of the left atrium is doubtful. The dense shadow above the bifurcation of the pulmonary trunk is a blind sac formed by the ductus arteriosus which was closed only at its junction with the aorta.

The duration of right heart opacification, fleeting in Fallot's tetralogy, but persistent in pulmonary stenosis with intact ventricular septum (Campbell and Hills, 1950), and the shape of the infundibulum, usually irregular in Fallot's tetralogy but smooth in pulmonary stenosis with intact ventricular septum (Soulié *et al.*, 1951*b*), are other features of value in differentiating these conditions. A right-sided aortic arch strongly favours the tetralogy.

SUMMARY

Intravenous angiocardiograms of fifty patients with Fallot's tetralogy are reviewed. In all cases a right to left shunt was demonstrated.

The area of pulmonary stenosis was seldom directly visualized. Reduction in the calibre of the pulmonary arterial tree gave indirect evidence of the stenosis in some cases, but in others no abnormality of the pulmonary arteries could be detected. Pulmonary stenosis did not cause delay in the filling of the pulmonary arteries and poor opacification of these vessels was exceptional. There was undue persistence of diodone in the pulmonary arteries but this was also observed in patients with severe pulmonary hypertension.

In eighteen cases the angiocardiographic appearances were correlated with the level of the stenosis which had been determined during intracardiac surgery or at necropsy. In this group the site of stenosis was clearly demonstrated by angiocardiography in only three, and in seven the films gave no indication of the level of the obstruction. In the remaining eight angiocardiograms the correct site of stenosis was suggested by indirect evidence.

The difficulties of angiocardiographic differential diagnosis between the tetralogy of Fallot and the Eisenmenger complex or pulmonary stenosis with a closed ventricular septum and reversed interatrial shunt are emphasized. Dense, early, left ventricular opacification is believed to favour pulmonary stenosis with intact ventricular septum and inter-atrial communication rather than Fallot's tetralogy.

I wish to express my thanks to the many registrars, radiographers, and members of the nursing staff who participated in these investigations at both the National Heart Hospital and the Brompton Hospital; to Dr. M. McGregor who initially instructed me in this technique; to Dr. B. G. B. Lucas who administered most of the anæsthetics; and to Mrs. I. O. Terry who prepared the illustrations. I am grateful to Dr. Maurice Campbell for his interest and advice. I am greatly indebted to Dr. Paul Wood for constant encouragement and for much helpful advice in the preparation of this paper.

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FATALITY FOLLOWING CARDIAC CATHETERIZATION INJURY

BY

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The widespread use of cardiac catheterization has revealed certain dangers inherent in the procedure when the catheter is advanced beyond the tricuspid valve. Ventricular and other ectopic rhythms are a well recognized risk, but less is known about the effect of damage to the endocardium produced by the catheter in man (Zimdahl, 1951). This paper presents in detail a case that terminated fatally, and the possible mechanism of such trauma is discussed in the light of this and other similar cases that have been reported.

Case Report

The patient was a male clerk, aged 44 years, who was suffering from calcareous mitral stenosis with pulmonary hypertension, and calcareous aortic stenosis. In view of his increasing dyspnœa on exertion and paroxysmal dyspnœa at rest, it was felt that mitral valvotomy was probably urgently indicated. Since the contribution of the aortic valvular lesion to his symptoms could not be fully assessed without hæmodynamic study, cardiac catheterization was advised.

After sedation with sodium amytal and local anæsthesia with procaine, a No. 9 American cardiac catheter was introduced into a left median antecubital vein and passed into the right atrium under fluoroscopic control, whence it was advanced into the main pulmonary trunk without difficulty. The catheter could not be further inserted into the right pulmonary artery and was therefore withdrawn a short distance for re-positioning. During withdrawal the tip slipped back through the pulmonary valve, and passed laterally to the left cardiac border (Fig. 1A). To determine its exact site, the patient was turned into the right oblique position and the catheter was seen to be pointing posteriorly (Fig. 1B). It was further withdrawn and then advanced gently and without difficulty through the pulmonary valve into the right pulmonary artery. The operator was experienced, and there was no undue resistance to the passage of the catheter. These manœuvres occupied approximately five minutes. Apart from occasional ectopic beats, the pulse was regular throughout. The patient said that he " felt fine," apart from a slight substernal ache. The pulse was of good volume, regular, and the rate had not changed. A few moments later he became pale, sweated, vomited, and complained of faintness; the pulse became slow (regular and at 50 a minute) and impalpable at the wrist. The systolic blood pressure rapidly fell to 40 mm. Hg. Severe hypotension and cardiac pain persisted for 12 hours, the pulse rate increasing to 120 a minute, and a pericardial friction rub being heard on the following day. Consciousness was maintained throughout, and the heart could be felt to be beating strongly.

He remained severely ill for the next 24 hours, but improved somewhat next day, the blood pressure rising to 130/80. A cardiogram immediately after the onset of the pain showed sinus tachycardia and increase in voltage of the T wave in V3, when compared with the previous tracing (Fig. 2A). A further tracing next day (Fig. 2B) revealed further increase in voltage of the T wave and S–T elevation consistent with pericarditis. The serum potassium rose to 8 m-eq. per litre, but returned to normal following glucose and insulin therapy. Distension of the abdomen, reduction in bowel sounds, and a copious vomit suggested acute dilatation of the stomach or paralytic ileus. In spite of treatment for acute circulatory failure, electrolyte imbalance, and ileus, he died suddenly, approximately 40 hours after catheterization. The jugular venous pressure remained normal and the lungs clear during the illness.

Necropsy. (Dr. C. V. Harrison.) The pericardium was flaccid and contained 150 ml. of fluid blood. Both surfaces were covered by a fine film of fibrin.

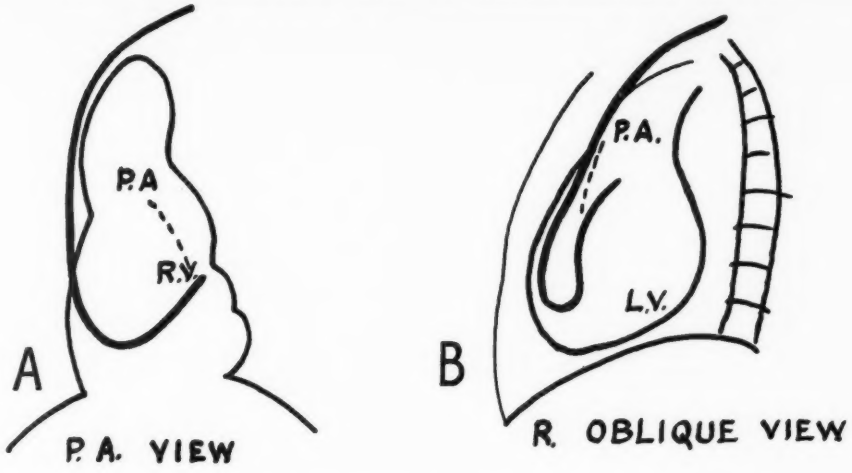

FIG. 1—Position of catheter in right ventricle after slipping back through pulmonary valve.

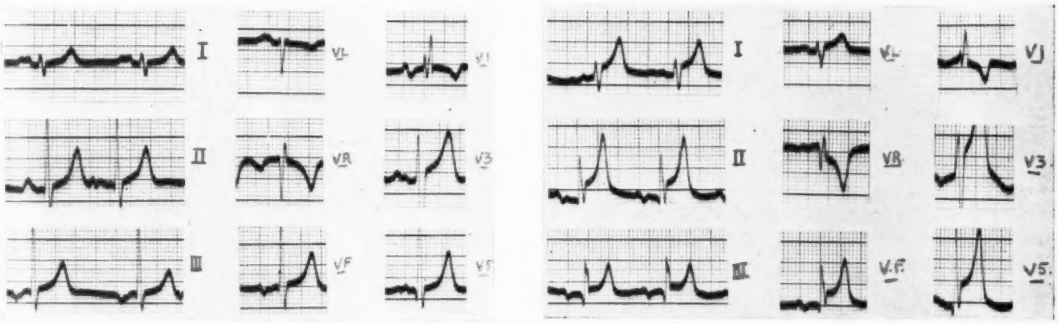

FIG. 2.—Cardiograms. (A) Before cardiac catheterization. Incomplete right bundle branch block and right ventricular hypertrophy. (B) 24 hours later. Increase in voltage of T wave in leads II, V3, and V5. Elevation of S–T segment 3–4 mm. in all leads, except VL, VR, and V1, indicating pericarditis.

Heart. 258 g. The right atrium was normal and the coronary sinus was healthy and free from signs of trauma or thrombus, as were the tricuspid and pulmonary valves. The right ventricle was not dilated but was hypertrophied to a thickness of 6 mm. in the conus region. There was a focus of hæmorrhagic discoloration in the epicardial fat over the right ventricle. This was about 15 mm. diameter and lay 5 mm. to the right of the descending left coronary artery, 35 mm. below the base of the aortic cusps. There was no sign of perforation of the muscle but the area of discoloration lay over a point where the ventricular cavity passed behind one of the larger columnæ carnæ (Fig. 3).

The left atrium was somewhat dilated and was moderately hypertrophied (2–3 mm. thick). The mitral valve showed gross stenosis, the posterior cusp and the two ends of the anterior cusps being calcified, and the chordæ tendinæ being fused.

The left ventricle was not dilated nor hypertrophied (15 mm. thick). The aortic valve was tightly stenosed and calcified.

Other organs. The stomach was dilated and contained 920 ml. of black fluid. There was some similar dilatation of the first and second parts of the duodenum but none in the rest of the intestine. The liver,

FIG. 3.—Photograph of the heart. (1) Pulmonary valve. (2) Right ventricular outflow tract. (3) Hæmorrhage into the epicardial fat overlying the endocardial lesion which lies behind the large columnæ carneæ. (4) Interventricular septum.

spleen and kidneys did not show any sign of passive congestion. The lungs were congested (right 760 g., left 620 g.).

Histology. Examination of the atrial muscle did not reveal any evidence of active rheumatism, nor was there any sign of ischæmic necrosis of the ventricular muscle supplied by the descending left coronary artery.

Sections taken from the area of suspected trauma all showed a little hæmorrhage into the subepicardial fat but only one showed any myocardial damage. Beneath one of the columnæ carneæ was a small endocardial thrombus (Fig. 4) old enough to have excited a slight infiltration of polymorphonuclears at its edge and of macrophages in the underlying endocardium. Adjacent to this was a small focus of recent muscle necrosis (measuring 350 × 800 μ) just beneath the endocardium. This appeared to be of about the same age as the thrombus. There were also a few torn muscle fibres but these had not excited any reaction and it was concluded that they were torn when examining the heart post mortem.

DISCUSSION

It is possible tentatively to reconstruct the course of events. On withdrawal of the catheter through the pulmonary valve, the tip moved laterally and became trapped behind the thick columnæ carneæ. In this position it may have been held firm while the ventricular wall contracted down upon it with each heart beat. This was sufficient to cause a small area of necrosis and bruising, with oozing of blood into the epicardial fat and into the pericardium. The delay of one to two minutes in withdrawing the catheter from this position, and rotation of the patient into the right oblique position where his heart could have been impaled upon the catheter, may well have contributed further to the production of the lesion. At no time was the catheter advanced with force against resistance.

The tiny myocardial necrosis and the small hæmopericardium would not seem to be sufficient to cause the rapid onset of irreversible circulatory failure, or the severe and prolonged cardiac pain.

FIG. 4.—Photomicrograph of the area of trauma, showing small endocardial thrombosis, without perforation.

However, the descending branch of the left coronary artery was very close to the lesion and if the trauma had resulted in spasm of this vessel, the clinical picture could be explained by acute coronary insufficiency. Moreover, patients with aortic stenosis are, in any event, liable to sudden attacks of coronary insufficiency which are sometimes fatal. There was no evidence of an arrhythmia or of cardiac tamponade. It seems possible that the patient might have recovered had he not developed acute dilatation of the stomach, which may have been connected with hyperkalæmia, produced by the release of potassium from tissue rendered ischæmic by the prolonged hypotensive state.

Undue stiffness of the catheter may have been a factor in causing the damage, although the instrument employed had been used many times previously without mishap. It is of interest that Ellis *et al.* (1950) found no correlation between the stiffness of the catheter and the severity of endocardial lesions in 16 dogs subjected to cardiac catheterization.

Although endocardial thrombosis occurs not infrequently in dogs after cardiac catheterization (Goodale *et al.*, 1947; Ellis *et al.*, 1950), there are comparatively few reports of the same complication in man, and in all save one the lesions have been confined to the right atrium, superior vena cava, or coronary sinus. The exception was a case of Ebstein's disease described by Holling and Zak (1950) in which a thrombus formed on the septal wall of the left ventricle (which had been catheterized via an atrial-septal defect) and produced fatal embolization ten days after catheterization. Biörck and Krook (1951) reported cardiographic evidence of a subendocardial injury and reduction in right ventricular pressures during catheterization, which they ascribed to myocardial injury by the catheter.

McMichael and Mounsey (1951) reported five non-fatal cases in which a syndrome identical with that described here occurred either during or immediately after cardiac catheterization. In

one of these, the electrocardiogram showed changes suggestive of pericarditis, and in two of lateral ischæmia; while in two there was no change. One patient developed a pericardial rub. All recovered so that the exact mechanism of the condition was not discovered, but it was suggested that deep catheterization of the coronary sinus was responsible. Further evidence in favour of this hypothesis was the position of the catheter, which in each case appeared to have penetrated deep into the coronary sinus, with probable perforation into the pericardial sac in one case. Further support was obtained from the work of Goodale *et al.* (1948) on dogs in which thrombotic occlusion of the great cardiac vein induced by the catheter had resulted in cardiographic changes of S–T segment elevation and T wave inversion. Possible penetration of the pericardium via the coronary sinus by the cardiac catheter in man has also been reported by Stern *et al.* (1952).

In view of the lesion demonstrated here it seems possible that damage to the endocardium of the right ventricle, rather than deep catheterization of the coronary sinus could have been responsible in some of the other cases.

It is difficult to see how this hazard can be avoided with certainty, but it is suggested that the tip of the catheter when in the right ventricle should be kept as far away from the lateral cardiac border as possible and that should it approach close to the edge of the cardiac silhouette, it should be withdrawn instantly. Furthermore, with the catheter in this position, the patient should probably not be rotated into the right oblique position. Finally, it should again be stressed that cardiac catheterization beyond the tricuspid valve is a serious procedure, which involves a significant risk of morbidity and even of mortality. In view of the increasing awareness of the dangers involved, it is felt that such catheterizations are only justified when the information derived can be used for the therapeutic benefit of the individual patient.

Summary

A case is described in which trauma to the endocardium of the outflow tract of the right ventricle, due to cardiac catheterization, resulted in death. Reference is made to similar clinical syndromes that have been separated, and suggestions are made for the prevention of such occurrences in the future.

I am most grateful to Dr. C. V. Harrison for his help with pathological data, and to Professor J. McMichael for his advice.

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NECROPSIES IN SOME CONGENITAL DISEASES OF THE HEART, MAINLY FALLOT'S TETRALOGY

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In spite of great progress in the clinical diagnosis of congenital heart lesions, especially with the help of cardiac catheterization and angiocardiography, these methods still fall short of complete proof and advances must be firmly based on fundamental facts of morbid anatomy. It has, therefore, been thought worth while to examine in detail the anatomy and pathology of this series of 55 necropsies made at Guy's Hospital between May, 1947, and March, 1950, on patients with congenital heart disease, especially as in most of them the history and clinical findings in life were well known.

Of the 55 cases, 25 consisted of Fallot's tetralogy and it is these that will be considered in most detail. There were 6 others with most of the features of Fallot's tetralogy but with pulmonary atresia; these have been fully reported by Allanby, *et al.* (1951) and reasons were given for separating them from Fallot's tetralogy because of the difference in their surgical treatment. The remaining 24 covered a wide range of developmental abnormalities (see Table II).

Fallot's Tetralogy

The twenty-five patients in this group are shown in Table I. Most were between 7 and 20 years of age. The classical characteristics of the tetralogy were clearly displayed in all these and the only instances in which further diagnostic comment is needed are Case 9, in which both the atrial and ventricular septal defects were so large as to amount to a bilocular heart (Case 5, Campbell *et al.*, 1953) but the infundibular stenosis and dextroposition of the aorta were characteristic enough to place it in this group, and Case 5, where the aorta arose entirely from the right ventricle and the ventricular septal defect was unusually small.

Emphasis was laid on displaying the abnormalities found, so when the heart was fresh the other mediastinal contents were kept attached to it and even in the final dissection the great vessels were usually left. The weight of the heart is, therefore, not always available but some idea of its size is given by the measurements of the thickness of the ventricular muscle and of the diameters of the aorta and pulmonary artery, all these measurements being made when the hearts were fresh.

Defects of the Atrial Septum. In 15 of the 25 cases there was no functional defect of the atrial septum; in many of these there was a slit- or probe-patency that was easy to distinguish from an effective patency. In the remaining 10 there was a functional defect: in Case 9 it was so large that there was hardly a septum and in Case 6 it was relatively large, but in the other nine it was not often more than 10 by 7 mm. or less than 6 by 3 mm. (see Table I) and averaged 9·2 by 4·7 mm. No correlation could be found between the presence and size of these defects and any other factor.

The Ventricular Septal Defect. This was strikingly similar in each heart, with the exception of Case 9 in which the septum was represented by a mere ridge at the bottom of an almost common ventricle, and Case 5 in which the defect was unusually small and the aorta arose entirely from the

right ventricle. The size of the defect was, with these exceptions, highly correlated with the size of the heart, the free upper border of the septum lying beneath the valves of the dextroposed aorta in the same relationship regardless of size. The transverse diameter of the defect averaged 13·6 mm. and was generally between 6 and 20 mm.

TABLE I

SOME MEASUREMENTS OF THE HEART IN FALLOT'S TETRALOGY

Case and reference No.	Sex and age	Ventricular muscle ratio R. (mm.)	L. (mm.)	L./R.	P.T. diam. (mm.)	Aorta diam. (mm.)	P.T/A. ratio	V.S.D. Transverse diam. (mm.)	Site of stenosis (mm. below pulm. valve and type)	The degree of overriding of aorta	A.S.D. diam. (mm.)	Weight of heart (g.)
1. (P01A)	M 19	16	11	69	10	15	67	10	20 Long inf.	—	Nil	—
2. (P012)	F 11	11	9	82	5	10	50	9	11 V.S. also	—	Nil	—
3. (P017)	F 7	9	8	89	5	15	33	11	11 Long inf.	—	Nil	—
4. (CB07)	F 9	7	4	57	7	13	54	12	8 Long inf.	—	Nil	—
5. (P054)	M 11	12	11	92	13	15	87	3	15 Inf.*	*	Nil	—
6. (P037)	F 7	14	13	93	4	16	25	14	10 Inf.†	—	14×9†	—
7. (H106)	F 7	9	7	78	9	19	47	7	6 High inf.	½	7×3	—
8. (O050)	M 4	10	9	90	8	16	50	18	20 Low inf.	½	4×7	—
9. (O086)	M 18	11	11	100	20	21	95	**	24 Inf.	—	**	—
10. (O115)	M 27	17	16	94	14	21	67	20	20 V.S. also	½	Nil	—
11. (H121)	F 24	15	14	94	12	23	52	16	V.S. only	—	Nil	—
12. (CB14)	F 12	13	11	85	9	15	60	9	11 Inf.	½	6×3	—
13. (P304)	F 6	9	8	89	8	13	62	6	12 Inf.	—	16×4	—
14. (O208)	F 14	9	6	67	6	13	46	8	18 Inf.	—	Nil	—
15. (P061)	F 36	11	8	74	13	17	76	14	18 Inf.	¼	Nil	—
16. (P023)	M 7	8	7	88	9	16	56	10	21 Low inf.	¼	Nil	100
17. (P063)	M 29	16	3	81	14	21	67	25	20 Inf.	¼	Nil	450
18. (O047)	F 5	8	4	50	7	18	39	12	27 V.S. also	¼	4×2	120
19. (O224)	F 20	12	10	83	14	17	82	18	19 Inf.	¼	9×3	270
20. (O246)	F 20	15	12	80	10	21	48	18	1 High Inf.	¼	10×4	360
21. (O377)	M 17	13	8	62	9	23	39	26	V.S. only§§	¼	Nil	280
22. (O373)	F 7	10	6	60	9	18	50	10	8 V.S. also	¼	10×10	93
23. (O029)	M 11	11	9	82	12	20	60	10	10 V.S. also	¼	Nil	180
24. (O133)	M 8	12	9	75	15	19	80	20	24 Multiple inf.	¼	Nil	310
25. (O448)	M 12	13	8	61	17	19	90	20	19 Inf.	¼	Nil	270

* Aorta arose entirely from R.V.: very small V.S.D. (Case 5).
† The heart was much larger than usual, and relatively the A.S.D. was the largest except for Case 9 (Case 6).
** The atrial and ventricular septa were almost absent, and functionally there was a single ventricle (Case 9).
§§ Died with bacterial endocarditis (Case 21).

Further, the appearance of the defect was similar in every case—a saddle-shaped ridge of muscle clothed with smooth and glistening endocardium that was not thickened or calcified, even in the older hearts in which these changes had occurred in the infundibulum to a greater or less extent. There were no vegetations attached to the defect in any case. This was particularly notable in Case 21 who was admitted with bacterial endocarditis and aortic incompetence superimposed on Fallot's tetralogy. Post mortem, a large tough vegetation, 25 mm. long and consisting of organized thrombus, was found attached to the ventricular surface of the anterior aortic cusp and extending well into the right ventricle: it must have caused great frictional trauma to the free upper edge of the ventricular septum, but the vegetations had nowhere seeded upon it and its endocardium was normal.

The Dextroposition of the Aorta. It is difficult to measure this precisely but, in all the later hearts and in some of the earlier ones an attempt was made when the hearts were fresh; it was based on the ease with which the aortic valve could be seen from the right and left ventricles respectively, checked by observation of the free edge of the ventricular septum seen from the aorta. This estimate is

expressed as a fraction—the degree to which the aortic ring over-rides the ventricular septal defect and thus lies over the right ventricle.

As in the other series, the degree of over-riding was very variable, the fraction expressed in this way being from one-quarter to seven-eighths, excluding Case 5, where it arose entirely from the right ventricle. It averaged three-fifths, or 60 per cent, showing that as a rule the aorta was rather more over the right than over the left ventricle. It was not possible to correlate this with any other anatomical factor in these hearts, but it is probably related to the degree of anoxæmia and cyanosis shown by the patient. Thus Cases 15 and 17, where the degree of over-riding was least, were 36 and 29 years old and had not been very cyanosed until the last years of their lives. Cases 21 and 25, however, where the aorta seemed to be mainly from the right ventricle were not more deeply cyanosed than some others.

Right Ventricular Hypertrophy. This has been recorded as the L.V./R.V. ratio, the thickness of the left ventricle as a percentage of the thickness of the right ventricle. The ventricular muscle was measured at a point mid-way between the apex of that ventricle and the tricuspid or mitral valve.

The average L.V./R.V. ratio was two-thirds. In other words, the thickness of the right ventricle was 50 per cent greater than the left instead of being much less. It averaged 11·6 mm. and was generally between 9 and 16 mm., while the average for the left ventricle was 7·8, with most between 6 and 12 mm.

Pulmonary Stenosis. The degree of stenosis (whether infundibular or valvular) can be expressed as the P.T./A ratio, the calibre of the pulmonary trunk as a percentage of that of the aorta. They were measured at a point 10 mm. above the aortic or pulmonary valves, except in the smaller hearts where a level somewhat nearer the valves was chosen. This method will, of course, over-estimate the size of the pulmonary trunk when the dilatation distal to a stenosis extends so far, but this was unusual.

The diameter of the pulmonary trunk averaged 10·4 mm. and was generally between 5 and 15 mm. The diameter of the aorta averaged 17·1 mm. and was generally between 13 and 21 mm. This gives a P.T./A ratio of 61 per cent and it was generally between 40 and 80 per cent instead of being the same size or a little larger.

The Site of the Stenosis. The outflow tract or infundibulum of the right ventricle presents the most variable and therefore the most interesting feature in these hearts, and though the series is small it contains most of the common variants. In the 25 cases, the stenosis was infundibular alone in 18, valvular alone in 2, and combined infundibular with valvular in 5: these figures are not representative (see later) probably because infundibular stenosis, provided the chamber is not too large, gives a picture that was more readily recognized as Fallot's tetralogy in 1947–48.

Infundibular Stenosis. The level of the infundibular stenosis can be high, intermediate, low, or multiple. It was generally between 5 and 24 mm. below the valve and on the average was 15 mm. below. A high infundibular stenosis could open from the sinus of the right ventricle immediately below the pulmonary valve, and an example of this is shown in Fig. 1. The infundibular portion of the right ventricle is then present as a chamber that extends downwards and superficially within the ventricular wall and terminates blindly at its lower end. Occasionally, with a high infundibular stenosis the infundibular cul-de-sac exists only as a potential space with the two endocardial surfaces closely apposed; more usually, however, it is a real chamber and is found to contain blood post mortem, although during life there was no current of blood through it.

At the other extreme those showing a low infundibular stenosis presented an orifice of greater or less calibre between the right ventricle and the outflow tract leading to the pulmonary valve on the left and anteriorly (Fig. 2 and 3). The outflow tract was often expanded above the stenosis, thus forming an infundibular chamber. In the older patients this was lined with endocardium that was commonly thickened, fibrous, or even calcified. Less commonly the infundibular chamber was long and narrow, though the stenosis remained low.

Between these extremes, the infundibular stenosis was found at various levels. The only striking example where it was multiple (Case 24) is described in some detail, for the tortuous passage

FIG. 1.—Drawing of a high infundibular stenosis. The pulmonary valve is normal, and almost immediately below it there is a fibrous infundibular stenosis without any infundibular chamber. The subclavian-pulmonary anastomosis is seen at the top of the figure. Case 20.

FIG. 2.—Drawing of a lower infundibular stenosis. The pulmonary valve is normal and there is a relatively large chamber below it. A fibrous infundibular stenosis is seen 24 mm. below the valve. The subclavian-pulmonary anastomosis is seen at the top of the figure. In this patient the infundibular stenosis shown was the upper fibrous ring and there was another below it (see text). Case 24.

by which blood reached the pulmonary trunk obviously raises difficulties in the surgical technique of direct attack on the stenosis—an operation that was in fact attempted. The outflow tract started as a short infundibular canal bounded below and above by fibrous rings, the first being circular and 8 mm. in diameter and the second oval and 8 by 5 mm. Between these rings the canal expanded chiefly to the left to form a chamber 9 mm. long, 18 mm. wide, and 14 mm. deep. After the second ring there was a second and larger infundibular chamber 24 mm. long, 26 mm. at its widest, and 12 mm. deep. It also expanded to the left, further and more superficially than the lower chamber, with which it was connected at its left-most and down-most extremity by a third very small fibrous ring, 3 mm. in diameter. It had also a diverticulum running for 10 mm. to the right to end blindly in the muscle of the right ventricle in its upper part, in front of the root of the aorta and not far from the A-V groove. The second chamber finally ended at the pulmonary valve ring which was normal (Fig. 2).

In most of these hearts there seems to be a small contracted infundibulum with much hypertrophy of the muscle, and these changes must add to the difficulty that the blood already has in reaching the lungs because of the localized fibrous ring. Undoubtedly, specimens examined post mortem have contracted and may exaggerate this impression, and Mr. Brock with his experience of feeling the infundibulum during life thinks that this is most important. On the other hand, some angiocardiograms and particularly those taken at short intervals, where the state of affairs during systole

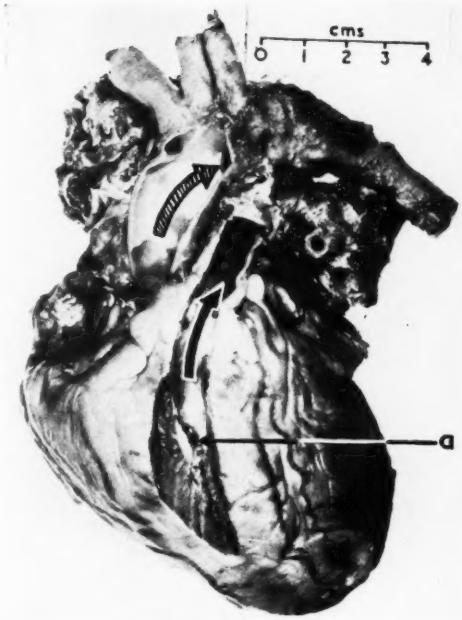

FIG. 3.—Photograph of a characteristic specimen of Fallot's tetralogy with a low infundibular stenosis (*a*). The black arrow indicates the flow through this to the pulmonary trunk and the hatched arrow the aorta. No operation had been performed. Case 14.

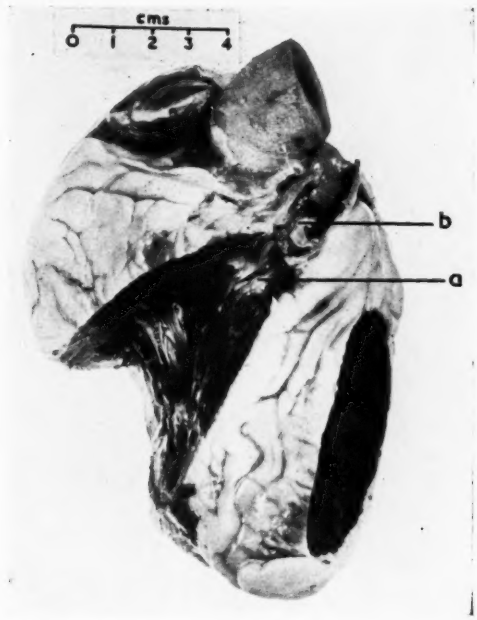

FIG. 4.—Photograph of the heart from a case of Fallot's tetralogy with infundibular stenosis (*a*) and valvular stenosis (b). There was unusually severe fibrosis and calcification of the pulmonary valve in this patient who had lived to the age of 27 years. Case 10.

and diastole can be distinguished, do show much narrowing of the whole infundibular region; it has been suggested that there is some under-development and abnormality of the infundibulum even in the cases where the stenosis is valvular only.

Valvular Stenosis, alone or with Infundibular Stenosis. In only two hearts out of the 25 was the stenosis wholly valvular (Cases 11 and 21). In both the opening between the right ventricle and infundibulum was wide and high so that the infundibulum could not be described as either a canal or a chamber: it was a relatively normal outflow tract bound distally by the stenosed valve. The valve in each case presented the familiar appearance of a conical diaphragm, convex on its pulmonary artery surface, with a small central orifice. In both the pulmonary trunk was dilated for a short distance distal to the valve and was thereafter under-developed, having the calibre about half that of the aorta.

A combination of infundibular with valvular stenosis existed in 5 of the 25 hearts; there was no consistency in the position of the infundibular stenosis, which might be high or low or intermediate. A photograph of a specimen with stenosis at both sites from an older patient is shown in Fig. 4. Another example is shown in Fig. 5 (Case 22): the infundibular stenosis (shown in the lower window cut in the infundibulum) was low in position, so that a chamber 8 mm. long existed between it and the stenosed pulmonary valve, which is sectioned longitudinally by the upper of the two windows. The valvular stenosis always had the same conical diaphragmatic form except that in Case 23 where it was not very severe it was eccentric, as it often is with congenital aortic stenosis (Campbell and Kauntze, 1953).

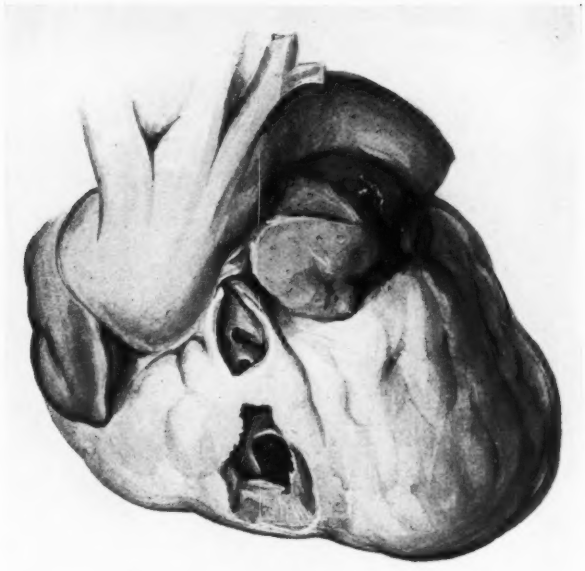

FIG. 5.—Drawing of a heart from a case of Fallot's tetralogy with valvular and infundibular stenosis. The pulmonary trunk is small and hidden. The upper window in the outflow tract of the right ventricle shows a conical-shaped pulmonary valvular stenosis that has been sectioned longitudinally. The lower window shows the infundibular stenosis that was 8 mm. below the valve. Case 22.

The pulmonary valve was often bicuspid. It was formed of two fused cusps only in both cases with lone valvular stenosis, and in two of the five where this was combined with infundibular stenosis: in the other three it was formed of three fused cusps. In the cases where the stenosis was infundibular only the pulmonary valve was formed of three cusps in eight cases and of two cusps in three. In Case 9 the aortic valve was also bicuspid.

Calcification of the pulmonary valve was unusual even when there was stenosis, but in Case 11, aged 24, the left cusp was distorted by thrombus and at the base by calcification which extended into the sinuses of Valsalva, and in Case 10, aged 27, the valve was extremely calcified and almost entirely occluded by recent thrombus.

Associated Abnormalities. Only two hearts presented abnormalities in addition to those of Fallot's tetralogy. In Case 17 a moderate degree of aortic valvular stenosis was present with complete fusion of the commissure between the anterior and left cusp and slight fusion of the other two commissures: the three cusps were normally developed, equal in size, and did not appear scarred or distorted, and the lesion was thought to be developmental. In Case 15, there was a slight constriction of the aorta that was thought to be without functional significance at the usual site of coarctation of the aorta.

Case 3 was an ordinary case of Fallot's tetralogy as far as the heart was concerned but the left pulmonary artery was completely occluded about 10 mm. from its origin, where it was joined by the ligamentum arteriosum. In Case 7, who had a right-sided aortic arch, the ligamentum arteriosum was not on the right but passed from the left subclavian to the left pulmonary artery.

Case 6 was the only one in this series where the congenital abnormalities seemed to be due to the mother having rubella during the second month of her pregnancy. In addition to the cardiac findings there was some mental defect and a congenital cataract of the left eye. A report from the Bristol Eye Hospital six years before described a constant rotary nystagmus, the left globe rather smaller than the right, and a dense lens opacity in the anterior cortex of the left eye; the child had two needlings with some lens swelling into the anterior chamber. When admitted for her operation Mr. Law found a right fixation nystagmus; pale eye grounds with engorged veins, probably an

albinoid basis; and opacity of the lens; the vitreous appeared clear and there was no microophthalmia.

Comment. Although the numbers are small it seems worth attempting to show some correlation between the different features of the tetralogy. There is a small but definite correlation between the severity of the pulmonary stenosis and of the right ventricular hypertrophy, and between the latter and the degree of dextroposition of the aorta. But the variations are unexpectedly wide and cannot be accounted for by such variants as the size of the ventricular septal defect, the position of the pulmonary stenosis, or the presence or absence of an atrial septal defect.

Site of the Stenosis in other cases. These and later necropsies in our patients during 1947–52 have included 10 with most features of Fallot's tetralogy but with pulmonary atresia and 48 with Fallot's tetralogy. Excluding the 10 with atresia, three-fifths of those with Fallot's tetralogy had infundibular stenosis only, one-fifth had infundibular and valvular stenosis, and rather more than one-fifth had valvular stenosis only.

In our earlier patients who had a subclavian-pulmonary anastomosis, the pericardium was not opened so the exact site of the stenosis is not known. Among our more recent patients operated on by Mr. Brock, Mr. Holmes Sellors, and Mr. Hill, there are 103 where the surgeon was reasonably satisfied about the site of the stenosis. Less than one-sixth of these had both infundibular and valvular stenosis, and about equal numbers of the remainder had valvular or infundibular stenosis.

In our 151 patients where the site of the stenosis was settled at necropsy or at operation, half had infundibular stenosis only, one-sixth infundibular and valvular, and one-third valvular stenosis only.

Donzelot *et al.* (1952) have described their surgical deductions from a study of 54 necropsies—10 with pulmonary atresia and 44 with Fallot's tetralogy. In one of the former (their number 185) the atresia was unusual because it was due to occlusion of the valve and would have been amenable to surgery—a condition we have seen for the first time only recently (Case O332). In one other there was a combination of this with severe infundibular stenosis and surgery might have been possible, but the others agree with the view we have put forward that the nature of the obstruction makes direct surgery impossible at present in pulmonary atresia (Allenby *et al.*, 1950). Of their 44 cases of Fallot's tetralogy there were only 4 with pure valvular stenosis, but 16 with valvular and infundibular stenosis. There were 24 with pure infundibular stenosis, one-fifth being high and one-fifth low and the remainder nearer the middle. Only a quarter of these showed an infundibular chamber of significant size. They distinguished 9 of the 44 cases as showing very little dextroposition of the aorta and 7 as showing this in an extreme form, the aorta in 3 of these coming almost entirely from the right ventricle as in our Case 5.

The Clinical Picture in Fallot's Tetralogy

Not much need be said about the clinical findings in these patients as they agree with those that have been given in other series. The patients were mostly between 7 and 20 years of age and were on the average (14 years) rather older than in most series, because they included a large proportion who died after operation and we have found the mortality increases with age after 20 years.

One point of interest is the relative fitness with subsequent deterioration of some of the older patients—a feature that is more common with pure pulmonary valvular stenosis. For example, Case 17, who was 29 when he died, was able to spend a long day in the field as a surveyor and was not greatly handicapped until three years before his death. He was suspected for this reason, of having a pure pulmonary stenosis though the relatively small heart favoured Fallot's tetralogy and this diagnosis was confirmed by angiocardiography. In his case the pulmonary valve showed unusual calcification but often increasing fibrosis follows the stresses and strains caused by the unusual anatomy and leads to more severe stenosis. Our general experience is that when a patient with pulmonary stenosis starts deteriorating, the end is not far away unless something can be done. Case 11, aged 24, became worse in the same way, but here the cause was thrombus on the valve, and it seemed that the passage must have become much smaller as the result of this in the last year or so.

All the patients had some degree of polycythæmia and the hæmoglobin percentages were between 110 and 180 and averaged 143 per cent. Eighteen of the 25 patients had squatted, most of them a great deal.

The Shape of the Heart. It is difficult to pick out any cardiac outline that will be found in all cases of Fallot's tetralogy. The most characteristic sabot-shaped heart is often seen in small children, but was present in few of these patients. We have selected four type teleradiograms, and most of the remainder resemble one or other of these fairly closely. In the first there is distinct hollowing of the pulmonary arc as when the heart is sabot-shaped, though it is minimized when it is small and central (Fig. 6). In the second this hollow has been filled in and the upper border is almost straight (Fig. 7). In the third the infundibular chamber causes some prominence of part of the left border (Fig. 8), and it may sometimes be much more than this. In the fourth there is more rounding of the lower left border from hypertrophy of the right ventricle (Fig. 9). The heart from Case 5, where the aorta arose entirely from the right ventricle, and the largest heart are shown in Fig. 10. When there is a valvular stenosis the pulmonary trunk and left pulmonary artery tend to be more prominent though not as much as with pulmonary valvular stenosis with a closed ventricular septum.

Case 6 was exceptional in showing a much larger heart than is usual in Fallot's tetralogy (Fig. 10B). It was sabot-shaped with a very deep, sharp pulmonary bay and a broad aorta—the picture that is characteristic of pulmonary atresia or truncus arteriosus—and in relation to the aorta the pulmonary trunk was much the smallest of the series. We thought the large atrial septal defect might explain this unusual picture, but cases with a single atrium do not generally show great cardiac enlargement and it does not seem possible that there was a large left-to-right shunt.

With this exception, the cardiothoracic ratio was never above 54 per cent and in nearly half it

FIG. 6.—A characteristic heart in Fallot's tetralogy. The heart is rather small and central with a blunt apex and a hollow pulmonary bay. From a girl, aged 14, with a cardiothoracic ratio of 46 (11·0/24 cm.). Case 14.

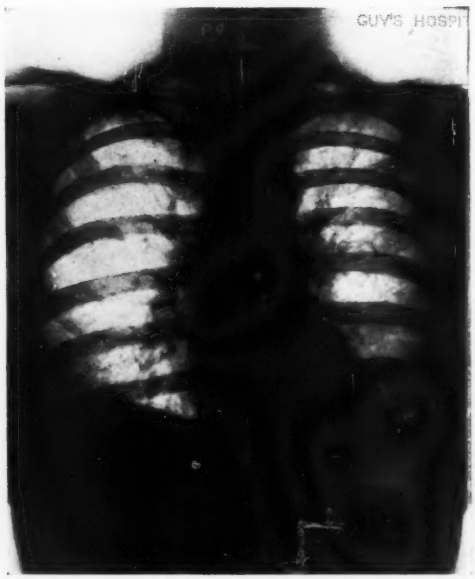

FIG. 7.—A characteristic heart in Fallot's tetralogy with a straighter left border. From a woman, aged 36, with a cardiothoracic ratio of 50 (11·7/23·5 cm.). Case 15.

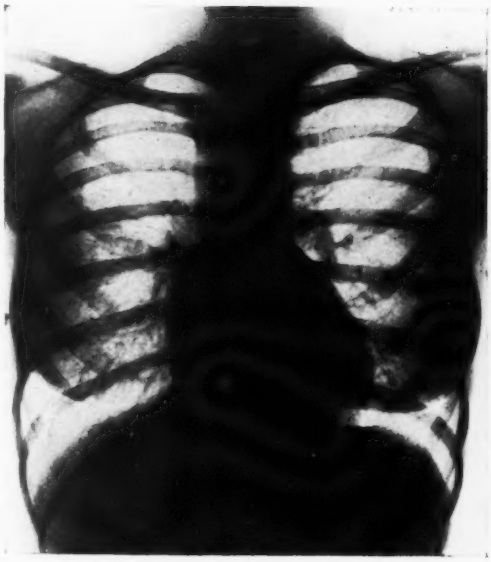

FIG. 8.—A characteristic heart in Fallot's tetralogy with slight prominence of the upper left border due to an infundibular chamber. From a woman, aged 20, with a cardiothoracic ratio of 49 (12·0/24·5 cm.). Case 19.

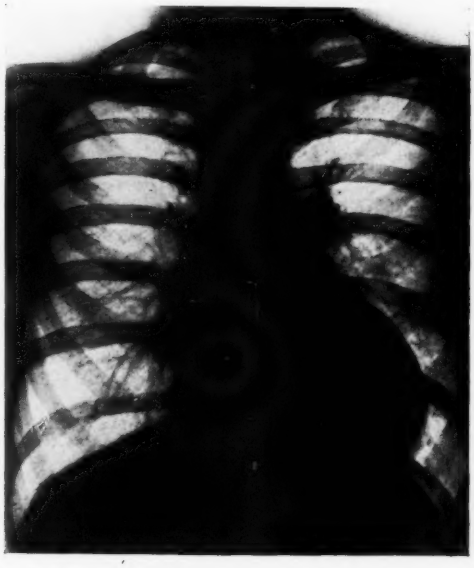

FIG. 9.—A characteristic heart in Fallot's tetralogy rather larger than the others; in uncomplicated cases the heart is not often larger than this. The aortic arch is right-sided. From a man, aged 29, with a cardiothoracic ratio of 52 (13·2/25·5 cm.). Case 17.

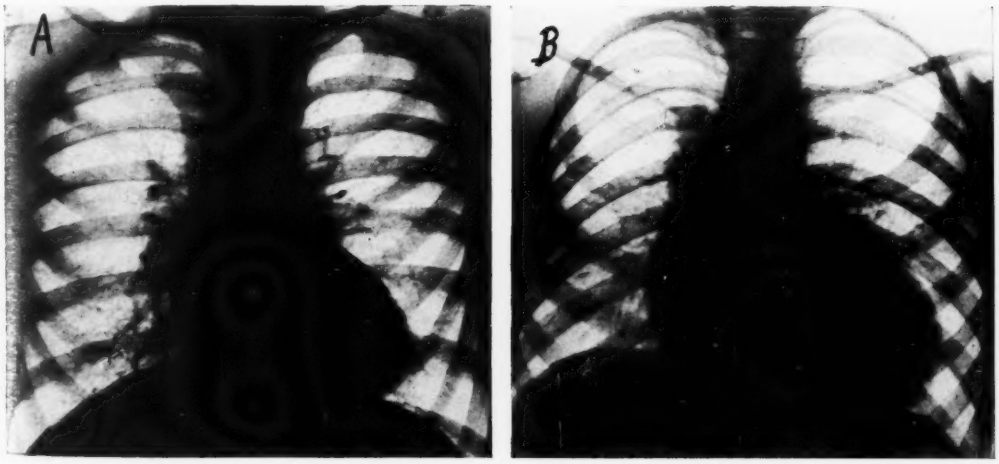

FIG. 10.—Teleradiograms from two less usual cases. (A) With the aorta arising entirely from the right ventricle, c.t.r. 53 (11·0/20·8 cm.), Case 5. (B) The largest heart with the picture that is seen more often with pulmonary atresia, from a patient who had Fallot's tetralogy with a very small pulmonary trunk and a large atrial septal defect, c.t.r. 63 (11·3/17·6 cm.). Case 6.

was between 45 and 49 per cent. We think that a cardiothoracic ratio above 54 should raise the question whether there is some other abnormality present. Brown (1950) has emphasized that the heart is generally normal in size or only slightly enlarged.

The aortic arch was right-sided in six of these cases, very close to the proportion of one-quarter that has been found so often.

Right ventricular enlargement is generally obvious on radioscopy, but rotation of the heart may simulate enlargement of the left ventricle as well in cases where it is not enlarged.

The Electrocardiogram. Right ventricular preponderance in the electrocardiogram is more constant and more reliable. All agree on its frequency in those diagnosed as Fallot's tetralogy, but a few such cases fail to show it. The present series does not help as regards these few exceptions, for there were none. We have not got chest leads in the earlier cases, but all where we have showed right ventricular preponderance. We have found that gross right axis deviation (small or more often insignificant RI and SIII and large RIII and SI) is almost the best evidence of right ventricular preponderance (Woods, 1952). With the single exception of Case 9, who had partial bundle branch block and almost a bilocular heart, all had gross right axis deviation as defined above, SI averaging 12 mm. and RIII averaging 13 mm.

Cases Other than Fallot's Tetralogy

A condition other than Fallot's tetralogy or pulmonary atresia was found in 24 of the 55 cases of congenital heart disease (see Table II). Seven of them were infants and had come to the post-mortem room with a clinical diagnosis merely of congenital heart disease, but the other 17 had been investigated more or less completely before death. Some of them have formed the subject of papers already published in *Guy's Hospital Reports* and to these no further reference will be made here. The two cases of *Ebstein's anomaly of the tricuspid valve* have been reported by Baker *et al.* (1950).

Six cases of *congenital pulmonary stenosis with closed ventricular septum* were reported in detail by Allanby and Campbell (1949), and there is one other to add. This patient (Case 40 of the present series), was a girl of 10 years who died shortly after pulmonary valvotomy. The heart weighed 370 g. (normal for age 120 g.) and there was the usual very great hypertrophy of the muscle of the right ventricle, its thickness being 9 mm. against 10 mm. for the left ventricle. Apart from this the right ventricle was normal up to the valve, which consisted of a diaphragm, convex upwards, formed from two cusps only. The valve-ring was normal in size (14 × 14 mm.), and the central opening had been dilated at operation so that it was not possible to estimate its natural dimensions. Above the stenosed valve the pulmonary trunk was dilated, having a diameter of 20 mm. as against 14 mm. for the aorta. There was a large atrial septal defect in the posterior and upper part of the septum.

Atrial Septal Defect

The six samples of this are described in two groups. The first, Cases 41–44, consists of four adults—all women. Two had mitral stenosis also and had been diagnosed as Lutembacher's syndrome, which was confirmed post mortem. Each had been in and out of congestive heart failure for more than a year before her death from this cause. The third (Case 43) lived to the age of 63 and, though a little breathless since school days, was hardly troubled by it until she was 49, when she had paroxysmal auricular fibrillation: when she was 54 fibrillation became established and she was more disabled, and from 60 to 63 she was often in hospital with congestive failure. The physical signs and the X-ray appearances were characteristic, and post mortem the atrial septal defect measured 50 by 35 mm.

Case 44. F., 32. The fourth remained well until her first pregnancy at the age of 31, when moderate dyspnœa and cyanosis in cold weather were first noticed. She developed œdema of the ankles, and in hospital was found to be cyanosed and polycythæmic (Hb., 17·2 g., red cells, 5·9 million) with some clubbing of the fingers. The heart was only moderately enlarged. There was palpable pulsation in the pulmonary area

TABLE II

CASES OF CONGENITAL HEART DISEASE WITH NECROPSY

Case No.	Diagnosis	Sex and age	Remarks
1–25.	Fallot's tetralogy	—	See Table I
26–31.	Pulmonary atresia	—	Reported fully by Allanby *et al.*, 1950
32–33.	Ebstein's anomaly of the tricuspid valve	—	Reported by Baker *et al.*, 1950
34–40.	Pulmonary valvular stenosis with closed ventricular septum	—	Cases 34–39 reported by Allanby and Campbell, 1949
40. (O041)	P.V.S. with closed V.S.	F10	With A.S.D.
41. (C201)	Atrial septal defect	F39	With mitral stenosis
42. (C223)	,, ,, ,, ...	F48	With mitral stenosis
43. (H312)	,, ,, ,, ...	F63	Without mitral stenosis
44. (C229)	,, ,, ,, ...	F32	Without mitral stenosis
45. (OA21)	,, ,, ,, ...	M7mo.	Anomalous great veins
46. (C215)	,, ,, ,, ...	F2mo.	Large P.D.A.
47. (OA18)	Tricuspid atresia	F2wk.	No other abnormality
48. (OA22)	Atresia of aortic arch	F6wk.	With V.S.D. and bicuspid aortic and pulmonary valves
49. (P083)	Single ventricle and infundibular stenosis	F8	Transposition of aorta and P.T. also
50. (P088)	Transposition of aorta and pulmonary trunk	F25	Infundibular stenosis
51. (O229)	,, ,, ,,	F7	Pulmonary stenosis
52. (O405)	,, ,, ,,	M3	Transposed abdominal viscera, P.S.
53. (P165)	,, ,, ,,	F8mo.	Isolated dextrocardia
54. (OA23)	,, ,, ,,	M3wk.	A.S.D. and P.D.A.: No V.S.D.
55. (OA14)	,, ,, ,,	M3mo.	A.S.D. and P.D.A.: No V.S.D.

and a systolic murmur, but no thrill was felt; the pulmonary second sound was accentuated. In spite of rest in bed the œdema persisted and after a month, as she was found to have albuminuria, Cæsarian section was performed; all went well for seven days, when she suddenly became gravely dyspnœic and died within half an hour. Post mortem, the cause of death was pulmonary embolism: the shape of the clot suggested that it had originated in the right atrium, and no thrombosis was found in the veins of the legs. The heart weighed 400 g. and there was great hypertrophy of the right ventricle. A defect in the atrial septum measuring 20 × 20 mm. was the only other abnormality.

The first three patients were acyanotic and only developed some peripheral cyanosis terminally with their heart failure. The fourth said she was cyanosed only in cold weather and only recently, but the polycythæmia and clubbing were unusual and suggested that there might have been an added right to left shunt or enough changes in the lungs to interfere with oxygenation. Unfortunately she was not studied by catheterization and the necropsy did not suggest there had been thrombosis in the lungs before her terminal illness.

The second group consists of two infants who died suddenly and apparently as a result of this defect, before any precise diagnosis had been made. It is of interest to enquire why this defect, which is usually without symptoms for many years, should sometimes lead to death in infancy. There must have been an unusually large left-to-right shunt through the large defect, though this is not necessarily so even when there is a single atrium.

Case 45. M., 7 months. The heart weighed 150 g. (normal for age 25 g.); this great increase was caused by the hypertrophy of the right ventricle, the thickness of which was 12 mm. compared with 4 mm. for the left. There was no ventricular septal defect and the infundibulum of the right ventricle was normal except that it was greatly dilated, as was the pulmonary trunk with a calibre of 14 mm. compared with 9 mm. for the aorta. The ductus arteriosus was large but had closed normally. The right atrium was dilated and was about six times the size of the left atrium. It received blood from a normal right superior vena cava and also from a left superior vena cava which entered it from the left side, through a coronary sinus that was so large that it looked like a triangular posterior extension of the right atrium pointing to the left. The left atrium was thus a small ill-developed structure wholly at the back of the heart; it received the four pulmonary veins normally. The small atrial septum lay in the lateral plane at the back of the heart and was also the site of a large defect measuring 17 × 10 mm.

Case 46. F. 2 months. The heart was very large and this was due to right ventricular hypertrophy. The pulmonary trunk was also very large. The atrial septum was normally placed but contained a large defect, 12 mm. in diameter. In addition, the ductus arteriosus was widely patent.

Miscellaneous Cases

There was one example of tricuspid atresia and one example of atresia of the aortic arch: both these died in infancy. This last condition, as pointed out by Taussig (1947), is closely related to the infantile type of coarctation of the aorta. The third case had a single ventricle and infundibular stenosis and an unusually primitive type of heart.

Case 47. F., 2 weeks. Tricuspid Atresia. This infant died on the twelfth day after birth. The enlargement of the heart was mainly due to the large left ventricle. The right atrium was almost isolated, its only exit being into the left atrium through a small patency of the foramen ovale: there was no tricuspid valve. The left atrium received the pulmonary veins normally and the mitral valve was normal. The left ventricle was the only functional ventricle; both aorta and pulmonary trunk arose from it with a normal relationship and without any stenosis or abnormality of either of their valves. There was a rudimentary right ventricle lying behind a small ridge on the right lateral wall of this single ventricle. The ductus arteriosus was open, but appeared from the wrinkled state of its intima, to be in the process of closing. There was an appreciable local narrowing of the aorta at a point just above the ductus.

Case 48. F., 6 weeks. Atresia of the Aortic Arch. This was an infant who had had attacks of cyanosis since birth, in one of which it died. When not in an attack there was only slight cyanosis of the face; and a greater degree of cyanosis in the lower part of the body had not been noted. The heart was enlarged and there was a loud systolic murmur over the whole præcordium.

Post mortem, the heart weighed 70 g. (normal for age, 20–25 g.) and many developmental anomalies were found. There was hypertrophy of both ventricular walls, the right measuring 7 mm. in thickness and the left 8 mm. A high ventricular septal defect of the Fallot type, measuring 10 mm., was straddled by a large pulmonary trunk (12 mm. in diameter) and by a hypoplastic aorta (6 mm. in diameter), the roots of these two vessels, bearing a normal relation to each other. The valves of both were bicuspid. Both atria were normal, and there was only a slit-patency of the foramen ovale. The hypoplastic aorta branched once only, to form the right innominate and left common carotid arteries. The pulmonary trunk, after giving off its main right and left branches, continued as a slender ductus arteriosus of only 2 mm. diameter and expanded distally to form the aortic arch (4 mm.) which gave off the left subclavian and left internal mammary arteries, and the descending aorta (5·5 mm.).

Both the aortic and pulmonary rings could be seen from the left ventricle, but the pulmonary was so much the larger of the two as to make it clear that in life blood flowed from the left ventricle through the septal defect into it. Thus the pulmonary trunk received blood from both sides of the heart and supplied the left arm and the lower part of the body though its only outlet besides the pulmonary capillaries was through the attenuated ductus.

Case 49. Single Ventricle with Infundibular Stenosis. This girl, aged 10 when she died, had been fully reported (Case 1, Campbell *et al.*, 1953). She had a single ventricle, infundibular stenosis, and transposition of the aorta and pulmonary trunk. The single ventricle makes the transposition of little clinical importance so she is grouped separately.

Transposition of the Aorta and Pulmonary Trunk

The remaining six are examples of transposition of the great vessels, and though they had this in common they differed in other ways and showed other abnormalities. The first three (and Case 49) had pulmonary stenosis and this modifies the general picture and in some ways makes it more like that of Fallot's tetralogy. A subclavian-pulmonary anastomosis was performed with temporary success in Case 49 and was attempted in Case 50, and was being considered in the other two when they died.

The other three had transposition without pulmonary stenosis: two of them had no ventricular septal defect and maintained their circulation through a small defect of the atrial septum and a patent ductus arteriosus—conditions that often lead to death in early infancy (Astley and Parsons, 1952) as in these cases.

There were other complex defects in some of the patients. Case 52 had transposition of the abdominal viscera and Case 53 had isolated dextrocardia. We have found, in examining hearts

of this sort, that the external appearance of the atria offers the best basis for judging the abnormal arrangement of the rest of the heart. There is generally one atrium that is larger and lies anteriorly and receives blood from the great veins of the body, and its companion is smaller, lies posteriorly, and receives blood from the lungs. These, of course, are normally the right and left atria respectively, but when there is transposition of the abdominal viscera they are often reversed. The sinus venosus appears to be the most stable part of the developing primitive cardiac tube, and the more anterior ventricular and bulbar portions seem more liable at first to abnormal torsion and later to defective absorption.

These cases of transposition also differed in the relationship of the aorta and pulmonary trunk. In Cases 49 and 50 the aorta was well to the right of and somewhat anterior to the pulmonary trunk. In Cases 51 and 52 it was almost directly in front of the pulmonary trunk and was hardly moved to the right. In Cases 54 and 55, and in Case 53 (allowing for the dextrocardia), the position was intermediate and the pulmonary trunk was also much nearer its normal size: these were the patients who had no pulmonary stenosis.

Case 50. M.S., aged 25 when she died, was unusual in having, in addition, both gout and thrombocytopenic purpura. She has been reported by Campbell and Suzman (1951), so only essentials of the anatomy are given here. At necropsy the heart was enlarged (400 g.) and the right ventricle was hypertrophied. There was a large defect of the upper part of the ventricular septum, 30 mm. in diameter. The pulmonary trunk over-rode this, slightly to the left of the aortic orifice. There was a low infundibular stenosis and bicuspid pulmonary valves. The pulmonary trunk was 10 mm. in diameter against 24 mm. for the aorta, which arose entirely from the right ventricle.

Case 51. C.L., a girl of 7, is being reported separately by Dixon, so only a summary will be given here. Partial transposition of the aorta and small pulmonary trunk both arising from the right ventricle. Pulmonary infundibular stenosis. Right (and left) atrial appendages to left of aorta. Atrial septal defect, 27 by 12 mm., (persistent ostium primum). Ventricular septal defect, 18 mm. in diameter, as in Fallot's tetralogy, but several smaller slits also. Common pulmonary vein.

Case 52. D.P., a boy of 3 years, is also to be reported separately by Brinton so is only summarized. Situs inversus with lævocardia. Anatomical transposition of the aorta and pulmonary trunk but both arising from the right ventricle, the only exit from the left ventricle being through the ventricular septal defect. Pulmonary infundibular and valvular stenosis.

Case 53. Isolated dextrocardia. Transposition of great vessels. Triloculate heart with single atrium and common A-V valve. The veins and atria normally related but the ventricles transposed.

M.D. was cyanosed and œdematous at birth, but only for 36 hours. She was admitted to Guy's Hospital under Dr. Evans at 4 months, when she weighed 8½ pounds. She was not cyanosed, but the hæmoglobin was only 68 per cent. The apex beat was in the mid-axillary line in the fifth *right* intercostal space, and there was an apical systolic murmur. The chest film and electrocardiogram confirmed the dextrocardia, but the liver and stomach were normal in position. She died at 8 months outside London and the heart was partly dissected and sent to us.

The external surface of the atria was normal, the right side being large and anterior and the smaller left side posterior. The atrial appendages were normal. The great veins were normal and entered the right side of the heart normally, as did the four pulmonary veins posteriorly. But within, there was a common atrial cavity. the septum being absent except in its uppermost part. The free border of this lay over a common A-V valve which possessed four cusps.

The right ventricle had the external appearance of a mirror-image left ventricle and was capacious and muscular (7 mm. thick) whereas the left, looking like a mirror-image right ventricle was smaller (5 mm. thick). The ventricular septum lay in an antero-posterior plane and was better developed than the atrial septum, but was deficient above and a cusp of the common A-V valve was attached to its free upper border.

The relationship of the great vessels was the opposite of normal, the pulmonary ring lying posteriorly and to the right and the aortic ring anteriorly and to the left. Neither of these was constricted below or at the valves, which were both tricuspid and normal. The diameter of the pulmonary trunk was 9 mm. and that of the aorta 8 mm. The aorta formed a right-sided arch and gave off left innominate and right carotid and subclavian arteries. The ligamentum arteriosum passed from the arch to the right pulmonary artery.

The coronary arteries reinforced the picture, the anterior being a mirror-image of the left, and the posterior a mirror-image of the right. The anterior arose from the centre of the right anterior aortic sinus and ran to the right for 6 mm., dividing into a descending branch which ran down the interventricular groove and a circumflex branch which continued to the right in the A-V groove. The posterior artery arose from the posterior aortic sinus close to its left commissure and ran to the left and posteriorly: after 23 mm. it divided into a descending branch which ran down in the interventricular groove posteriorly, and a circumflex branch which continued round in the A-V groove.

Case 54. Transposition of the great vessels. The greater and lesser circulations separate except through a trivial A.S.D. and a large P.D.A. No V.S.D.

M.P. was born in Guy's Hospital: he was not cyanosed at birth but severe cyanosis developed on feeding and continued till his death from congestive heart failure on the twenty-third day. A harsh systolic murmur was heard over the præcordium.

The external appearance of the heart was normal, except for the dilatation of the right ventricle. The great veins, the pulmonary veins, and both atria were normal. The atrial septum was normal except for a small ostium secundum, measuring 1 × 2 mm. The right ventricle was hypertrophied and dilated (4 mm. thick) and its outflow tract joined the aorta, whose ring lay anteriorly and to the right. The left ventricle was smaller (2 mm. thick), and its outflow tract, which showed an infundibular stenosis of moderate degree, led to the pulmonary ring which lay posteriorly and to the left. The A-V valves were normal and the ventricular septum contained no defect. The aortic arch was left-sided and there was a widely patent ductus arteriosus (3 mm.) between the aorta and the left pulmonary artery. The diameters of the aorta and the pulmonary trunk were 4 mm. and 3 mm. respectively.

Case 55. Transposition of the great vessels. The greater and lesser circulations separate except through a trivial A.S.D. and a P.D.A. of normal dimensions. No V.S.D.

T.McD. was admitted to Guy's Hospital for dyspnœa and cyanosis on exertion. A systolic murmur was audible all over the præcordium. The chest film confirmed the enlarged heart and pleonæmic lungs. The liver was enlarged and there were crepitations at both lung-bases. The cardiogram showed right ventricular preponderance and a large and pointed PII. The pyrexia continued and he died when three months old, from intracranial hæmorrhage complicating pyelonephritis.

The heart was greatly enlarged, especially the right atrium and ventricle. The right atrium received the great veins normally, the septum showed a slit-patency only, and the tricuspid valve was normal. The right ventricle was hypertrophied and dilated and the outflow tract led to the aortic ring which was situated to the right and posteriorly. There was no defect of the ventricular septum. The left atrium received the pulmonary veins normally and the mitral valve was normal. The left ventricle gave origin to the pulmonary trunk though it was more normally situated to the left and anteriorly. The ductus arteriosus was patent but not large, and the branches of the aorta, including the coronary arteries, were normal.

Summary

There were 55 necropsies at Guy's Hospital in 1947–50 on patients with congenital heart disease. Twenty-five of these were examples of simple Fallot's tetralogy and have been described fully. The general picture is very similar in each case though there is a good deal of variation in detail.

A functional defect of the atrial septum, about 9 by 5 mm., is present in more than one-third, but does not seem to make any difference to the clinical picture. The ventricular septal defect is nearly always just below the valves and is bounded below by a saddle-shaped ridge of muscle clothed with smooth endocardium: its size corresponds with the size of the heart and is commonly between 10 and 16 mm. in transverse diameter.

The aorta always over-rides this except in the rarer cases where it arises entirely from the right ventricle, and the degree to which this happens varies between one-quarter and seven-eighths, and averages three-fifths, i.e. more over the right than over the left ventricle. The right ventricle is always hypertrophied and is commonly 50 per cent thicker than the left, averaging nearly 12 mm. against 8 mm. for the left.

The pulmonary trunk is smaller than the aorta, generally between 40 and 80 per cent of its size, instead of being about the same; the average diameters were 10 mm. and 17 mm. Taking our figures from a more extensive series the stenosis is infundibular alone in one-half, infundibular and valvular in one-sixth, and valvular alone in one-third. When it is infundibular, the site is commonly from 5 to 25 mm. below the valve and is sometimes multiple: there is generally a fibrous ring, but the whole tract is narrow and under-developed. When it is valvular it has the familiar appearance of a conical diaphragm with a small central orifice, and has developed from two cusps or from three cusps in about equal numbers of cases.

The clinical picture of these patients with Fallot's tetralogy has been referred to shortly, and the commoner X-ray appearances have been described. The classical sabot-shaped heart is not very common except in infants and there is much variation in the shape and appearance of the heart, but most resemble one of four types illustrated. Right ventricular enlargement is generally obvious

on radioscopy, but rotation of the heart may simulate enlargement of the left ventricle as well. Right ventricular preponderance in the electrocardiogram is more constant and more reliable.

Six other patients had the general features of Fallot's tetralogy but with pulmonary atresia instead of stenosis. Seven had pulmonary valvular stenosis with a closed ventricular septum: all but one of these had a right-to-left shunt through the atrial septum. Two had Ebstein's anomaly of the tricuspid valve. These three groups have been described elsewhere.

Six others had an atrial septal defect. Three of these, two of whom had mitral stenosis also, lived to middle age and the fourth with a very large defect was hardly inconvenienced till she was 49 and lived to 63 years of age. The other two with very large defects and great right ventricular hypertrophy died in infancy.

There were single examples of tricuspid atresia and of atresia of the aortic arch: both these died in infancy. One patient had an unusually primitive type of heart with a single ventricle, infundibular stenosis, and transposition of the aorta and pulmonary trunk. Six others had transposition, three with and three without pulmonary stenosis. Most of them died in infancy, but one with pulmonary stenosis lived 25 years. One had in addition isolated dextrocardia and another had transposed abdominal viscera.

We should like to thank those who have worked with us on the patients with congenital heart disease, especially the late Dr. G. D. Channell. His knowledge of anatomy and embryology made him an ideal colleague for this work and the measurements of the earlier cases were mostly his. His death in an explosion at the Brompton Hospital while he was working on one of these specimens was a tragic loss.

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CATION EXCHANGE RESIN (RESODEC) IN THE TREATMENT OF CARDIAC ŒDEMA

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Cardiac œdema has long been attributed to increased intracapillary pressure secondary to raised venous pressure, but in recent years the role of sodium in the formation of œdema has received increasing attention. Peters (1935), Best and Taylor (1937), and Gamble (1937) pointed out that retention of sodium in the tissue spaces promotes the accumulation of water. Brod and Fejfar (1950) suggested that cardiac œdema depends, not on changes in venous pressure, but on renal vasoconstriction with diminished renal blood flow and consequent retention of water and salt. On the other hand, Dock (1949) reported that the rate of œdema formation is determined more by sodium ingestion than by reduction of cardiac output and renal blood flow. As a corollary to these concepts there arose the idea of sodium restriction as a therapeutic measure.

In common with other investigators we have had numerous gratifying results from a diet yielding a daily intake of 800 mg. sodium in refractory or relapsing congestive failure. Many of our patients had been œdematous and bedridden for periods up to six months prior to dietetic treatment: they have become free from œdema and ambulant, in several instances for as long as three years. In these refractory cases it is necessary to continue sodium restriction indefinitely: several patients have had recurrence of œdema within a few days of relaxing the diet. Cameron (1949) gave salt to patients whose œdema had been abolished by digitalis, diuretics, and low sodium diet: 2 grams of salt or sodium bromide daily (400 mg. sodium) caused a significant increase in weight almost immediately. This increment corresponds to a change from a " low sodium diet " to a " salt free diet."

Dietetic sodium restriction has several disadvantages. The food is apt to be savourless. As a domiciliary treatment it requires separate cooking for the patient and it is usually impracticable during holidays. The diet is deficient in chloride as well as in sodium; it necessitates the taking of ammonium chloride or hydrochloric acid, to which some patients object strongly. Finally, if supplementary chloride is not taken in adequate amount, it may cause dangerous sequelæ (Black and Litchfield, 1950), a risk that is intensified when mercurial diuretics are used as well. The disadvantages have stimulated research, notably in America, on the possibility of achieving sodium deprivation by means of ion exchange resins.

Clinical use of ion exchange resins was first suggested by Segal *et al.* (1945) using anion exchange resins for the control of gastric acidity in peptic ulcer; a year later Dock (1946) gave a cation exchange resin to rats and dogs orally, showing that it was non-toxic and that it increased the fæcal excretion of sodium. Two main groups of resins have been tried clinically—sulphonic resins by Kahn and Emerson (1950), MacIntyre and Jordan (1951), Morton (1951) and Friedman *et al.* (1951); carboxylic resins by Cobbey *et al.* (1949), Kahn and Emerson (1950), Chapman and Pannill (1950), Martz *et al.* (1950), Zatuchni (1951) and Kleiber and Pickar (1951). The earlier resins exchanged hydrogen ions for sodium and potassium; they occasionally produced hypokalæmia. Combined ammonium and potassium resins were accordingly introduced; these have 20 per cent of their hydrogen ions replaced by potassium and 80 per cent by ammonium. In the acid gastric contents they exchange

ammonium and potassium for hydrogen ions. The potassium compensates for that absorbed in the alkaline contents of the intestinal tract: here the resin exchanges hydrogen for sodium, potassium, and calcium ions which are excreted with it in the fæces. The use of combined ammonium and potassium resin in cardiac œdema has been reported by Irwin *et al.* (1949), Hay and Wood (1950), Dock and Frank (1950), Chapman and Pannill (1950), McChesney (1950), Flannagan *et al.* (1951) and Lefken *et al.* (1951). In patients with impaired renal function, ammonium chloride liberated in the stomach may give rise to acidosis, but apart from this few serious side effects were observed; the resin was considered to be of value in congestive heart failure and in cirrhosis of the liver.

Material and Methods

The therapeutic trial was made with a balanced ammonium-potassium form of carboxylic cation exchange resin (resodec). As subjects we chose ten patients with refractory or recurring congestive heart failure. Seven had been on treatment with low sodium diet for periods varying from several weeks up to two years; their individual clinical and biochemical response to variations in the sodium content of the diet was well known to us. Prior to dietetic treatment they had either failed to respond to routine digitalis and mercurial diuretic treatment: or œdema had recurred on withdrawal of mercurials or when the patient was allowed up. The diet had a calculated sodium content of 700 mg. daily, but analysis on several occasions showed an average sodium content of 800 mg. Supplementary chloride was given as ammonium chloride (45 to 60 gr. daily) or as dilute hydrochloric acid (10·6 c.c. daily), the dosage being varied in accordance with the plasma chloride level. Four of the seven became œdema-free and ambulant, remaining so for as long as they adhered to the diet; but œdema returned whenever they took ordinary diet. Three of them were treated with resodec when they next developed œdema; the fourth was given increasing doses of salt until he developed œdema and was then given resodec. Two other cases were responding slowly to diet when resodec was given with the object of accelerating the loss of œdema. In the seventh patient, œdema could be reduced but not abolished by diet; resodec was used in addition to the diet. Three other patients who would ordinarily have been selected for dietetic treatment were instead given resodec.

The dosage of resodec was 45 g. daily in three doses, except in one case where varying doses were tried; 30 g. daily produced no improvement while 60 g. gave no better result than 45 g. and was less well tolerated, a finding that agrees with the experience of previous observers. The resin was given in tea, fruit juice, or milk. Additional calcium was provided, in one case as calcium gluconate and in the remainder as extra milk. Fluids were not restricted. Weight, urinary output and urinary chlorides were recorded daily, but the weight records covering four courses of treatment are not available; blood electrolytes were estimated weekly in all cases, twice weekly in some. In one patient sodium balance experiments were carried out and in two others the urinary excretion of sodium was estimated.

The ten patients between them received fourteen courses of resodec treatment, varying in duration from 3 to 18 days. In nine instances the resodec was given with ordinary ward diet, as a substitute for low sodium diet; in five it was used as a supplement to low sodium diet with a view to producing a greater degree of sodium restriction.

Results

We would emphasize at the outset that we deliberately chose patients who had previously proved refractory to routine digitalis and mercurial diuretics. Table I gives the clinical result of fourteen courses of resodec treatment in such cases, compared with the effect of previous dietetic sodium restriction when known.

Weight and œdema. Body weight was reduced in nine of the ten cases in which weight records were available and presumably in two of the remaining four. The reduction amounted to 0·9 kg. daily in one case, 0·67 kg. daily in one, and approximately 0·45 kg. daily in four. Œdema was abolished in four, lessened

in seven, and unchanged in three. Case 1, who gained 4·5 kg. in 21 days with low sodium diet plus added salt, lost the same amount in 10 days on ward diet plus resodec. Case 3 had gross œdema which failed to clear after several weeks' treatment with digitalis and mersalyl; low sodium diet reduced the bulk of her œdema and ascites but there remained œdema of the thighs which began to increase slowly when she was allowed up. Her minimum weight on low sodium diet was 57·6 kg.; when given resodec as a supplement to low sodium diet, her œdema was reduced to an insignificant trace and her weight fell to 52·2 kg. in 9 days. On withholding resodec her weight rose and œdema returned. She was given two more short courses of resodec while in hospital, on each occasion with loss of weight and reduction of œdema. For the next nine months she kept herself ambulant by continuing the diet and taking resodec for three days at a time whenever her weight rose to 54·9 kg.; she died while on holiday some 200 miles from home.

TABLE I

CLINICAL EFFECTS AND SIDE-EFFECTS OF RESODEC

Case	Sex	Age	Diagnosis	Trial	Previous effect of low sodium diet	Duration and effect of resodec treatment			
						Days	Œdema	Weight	Side-effects
Cases previously treated by low sodium diet; now resodec + low sodium diet									
3	F.	64	RHD	1	Œdema reduced	9	Much less	−5·4 kg.	Hyperchloræmia and mild dyspepsia
				2	Returning œdema	4	Reduced	−2·25 kg.	Hyperchloræmia and mild dyspepsia
				3	Returning œdema	3	Reduced	−0·45 kg.	None
4	M.	47	SHD		Œdema abolished but delirium	11	Abolished	−7·2 kg.	No biochemical change: delirium
9	F.	48	HHD		Œdema reduced	5	Much less	−4·5 kg.	Hypokalæmia—sick, weak and confused
Cases previously treated by low sodium diet; now resodec + ordinary ward diet									
1	M.	64	HHD		Œdema abolished	10	Abolished	−4·5 kg.	Hyperchloræmia, acidosis
2	F.	41	RHD		Œdema reduced	18	Reduced	−1·35 kg.	Mild hyperkalæmia and diarrhœa
6	F.	63	HHD		Œdema slowly reduced	12	Abolished	−5·4 kg.	Hyperkalæmia, hyponatræmia, transient diarrhœa and vomiting
8	M.	57	RHD	1	Abolished	10	Abolished	−1·35 kg.	None from resin; digitalis intoxication
				2	Returning œdema	11	Unchanged	—	None from resin; no improvement. Died 11th day
Cases not previously treated by low sodium diet; resodec + ordinary ward diet									
5	F.	64	IHD		—	5	Much less	—	None. Sudden death (coronary) 5th day
7	M.	55	RHD		—	8	Unchanged	—	Hypokalæmia but none subjective. No improvement (just after lung infarct.) Later control by LSD
10	M.	68	IHD	1	—	14	Much less	—	None
				2	—	7	Unchanged (minimal)	+0·45 kg.	None. Later kept œdema free by LSD

LSD = Diet containing 800 mg. sodium daily with 45–60 gr. NH_4Cl.
RHD = Rheumatic heart disease.
SHD = Syphilitic heart disease.
HHD = Hypertensive heart disease.
IHD = Ischæmic heart disease.

Urine. A reduction in weight and œdema brought about by resodec was not necessarily accompanied by diuresis. The average daily output remained unchanged during eight courses of treatment, in seven of which weight was lost and œdema lessened. This is contrary to our experience with dietetic sodium restriction which usually produces a decided diuresis. Mild diarrhœa occurred in one of these cases and vomiting may explain the absence of diuresis in a second; but four patients lost weight and œdema without diuresis, diarrhœa, or vomiting. Nevertheless the gastro-intestinal tract seems the most likely route of the fluid loss.

Urinary sodium excretion was estimated in two patients before and during resodec treatment. Case 1, who lost 4·5 kg. in weight, showed a progressive rise in sodium excretion from 113 to 211 milli-equivalents per day while on resodec. Case 2 lost 2·2 kg. in weight and her sodium excretion rose from 54 to 88 m-eq. per day during the first three days on resodec; during the next three days sodium excretion fell to 58 m-eq. per day and weight increased 0·9 kg. though treatment was unchanged. On increasing the dose of resodec to 60 g. daily the sodium excretion dropped still further, to 39 m-eq. per day and weight rose another 0·45 kg. Case 6, who lost 5·4 kg. in weight excreted 96 m-eq. daily for the first three days and 88 m-eq. daily for the second three days as compared with 61 m-eq. daily during a subsequent period of dietetic sodium restriction. These findings suggest that urinary sodium excretion rises during periods of weight reduction in response to resodec, but may fall when weight reduction ceases or is reversed.

The urinary chloride excretion increased when resodec produced loss of weight and diminution of œdema. An appreciable fall in chloride excretion occurred in two patients in whom resodec failed to lower weight or reduce œdema. The explanation offered is that the resin absorbs sodium from the sodium chloride of the diet leaving the chloride to be absorbed by the patient, presumably in the form of its ammonium salt. This will increase the urinary chloride excretion unless the chloride is fixed by sodium in the tissues, in which case œdema will persist or increase. A considerable rise in urinary chloride excretion is sometimes insufficient to prevent hyperchloræmia.

Plasma chloride. Figures for the plasma chloride level before and after treatment are available for 11 courses. The final plasma chloride level was higher than the initial level in 9 instances (Table II), while

TABLE II

EFFECT OF RESODEC ON BLOOD ELECTROLYTES

Case	Days on resodec	Serum sodium		Serum potassium		Plasma chloride		Alkali reserve	Blood urea
		Before	After	Before	After	Before	After		
2	18	344→322→340		24·1	26·1	501→530→558→546		44→54	22→39
10, 1st	14	315	330	20·1	23·1	521 →568→	516	64→63	61→43
6	12	336→323→308		20·4→38·3→40·2		542	553	57→47	29→53
4	11	318	322	23·9	18·2	574	579	39→73	63→48
8, 2nd	11	330	328	22·9	19·1	540	574	— —	— —
1	10	336	344	23·4	21·9	597	667	45→26	70→67
8, 1st	10	334	334	20·9	21·7	572 →603→	571	— —	— —
3, 1st	9	328	344	22·9	20·9	578	645	61→46	38→32
7	8	—	335	—	15·4	—	521	— 41	— 25
10, 2nd	7	330	343	18·4	22·5	557 →552→	570	56→55	42→42
5	5	338	—	22·7	—	550	—	64 —	40 —
9	5	327	327	17·4	18·2	555	604	48→45	25→18
3, 2nd	4	332	340	23·9	18·2	582	631	87→56	34→32

Case 5 died suddenly (coronary disease) before second blood sample was taken. No blood sample available before start of treatment in Case 7.

Figures expressed in mg. per 100 ml. Alkali reserve in vols. CO_2 per 100 ml.

in the remaining two there was an initial rise followed by a fall. In four cases the initial plasma chloride level was low (501, 521, 540, and 542 mg. per 100 ml.) in consequence of previous low sodium diet or mersalyl: the rise during resodec administration brought these cases within or near the normal range. On three occasions hyperchloræmic levels were reached (631 to 667 mg. per 100 ml.): the highest of these values was assoicated with a drop in CO_2 combining power from 45 to 26 vols. per 100 ml.

The effect of resodec on plasma chloride is the reverse of that of low sodium diet. Dietary sodium occurs mainly in the form of chloride and bicarbonate; a diet poor in sodium is also deficient in chloride. One of the main problems with low sodium diet is to prevent a fall in plasma chloride which may precipitate an Addisonian crisis with hypotonia, asthenia, mental symptoms, and even death. It is likely that patients whose plasma chloride level cannot be adequately maintained on low sodium diet will prove amenable to resin therapy, while those who become hyperchloræmic with resin therapy will respond better to diet. We have not had an opportunity of testing the former thesis, but have had success with low sodium diet in a case of the latter type.

Serum sodium. Table II gives the serum sodium levels before and after treatment in 11 courses. In eight the serum sodium was within the normal range both before and after treatment; the figure rose

slightly in four cases, fell slightly in one, and remained stationary in three. Two patients had subnormal serum sodium before treatment, with normal values at the end of the course. In one patient the level fell from normal (336 mg. per 100 ml.) to a hyponatræmic value (308 mg. per 100 ml); the serum potassium rose simultaneously from 20 to 40 mg. per 100 ml.; the patient had transient diarrhœa and vomiting; normal values were regained within two days of stopping the resin treatment and a tendency for œdema to recur was easily controlled by low sodium diet.

Serum potassium. In seven patients (six of whom had previously been on low sodium diet) the serum potassium was slightly elevated before starting resodec therapy. In five of these the level fell during administration of the resin and was normal at the end of treatment. One with coronary disease died suddenly before the second blood sample was obtained. In the seventh the level continued to rise from 24 to 26 mg. per 100 ml.; the blood urea rose simultaneously from 22 to 39 mg. per 100 ml., and the rising serum potassium may have been a manifestation of incipient renal decompensation. In four instances the initial serum potassium was normal; one remained normal, two rose to levels just beyond the normal range without any rise in blood urea, and one became doubled, rising from 20 to 38 mg. per 100 ml. in 7 days and to 40 mg. per 100 ml. on the 12th day; the blood urea rose from 29 to 53 mg. per 100 ml. This was a case of hypertensive heart failure in which renal function was known to be defective. Two days after withdrawal of the resin the blood potassium was 18 and blood urea 46 mg. per 100 ml. After another 3 days she was given 30 g. of resodec in two doses; on the following day her serum potassium was 30·7 mg. per 100 ml. and nausea recurred. In one patient the initial serum potassium level was slightly subnormal; hypokalæmic symptoms appeared as soon as the resin was given though the serum potassium level was virtually unchanged at the end of the period of treatment. Finally, a patient whose serum potassium was not estimated prior to treatment was found to have a symptomless hypokalæmia with 15·4 mg. potassium per 100 ml. on the eighth day.

Sodium balance. This was estimated in Case 1 over a period of 56 days during which differing regimes were tried (Table III). He had already been on low sodium diet, without supplementary chloride, for 15 days when the investigation began. For the first 5 days urinary sodium excretion was slowly rising and he was in negative sodium balance. Addition of hydrochloric acid increased the sodium output; for the next 8 days the urinary sodium loss was double the intake. Hydrochloric acid was now replaced by sodium chloride, 2 g. daily for 7 days, 3 g. daily for 10 days, and 4 g. daily for 5 days. Addition of 2 g. of salt daily raised intake and excretion equally; the patient remained in negative balance but to a less extent than before and his weight increased from 64·8 kg. to 66·6 kg. With 3 g. daily the sodium excretion fell slightly and he went into positive sodium balance. With 4 g. daily the excretion rose a little, but not sufficiently to balance the increased intake which now exceeded output by one-sixth. Ward diet was next given with unrestricted salt; the exact sodium intake is not known but it was certainly greater than with low sodium diet plus 4 g. added salt: although sodium excretion rose the weight also increased. Resodec was now started. After an initial drop on the first day the sodium excretion rose steadily from 113 to 211 m-eq. per day; negative sodium balance was re-established and was accompanied by a drop in weight from 68·4 kg. to 63·9 kg. and disappearance of the œdema which had developed during the "added salt regime." The serum sodium changed but little during resodec administration; but plasma chlorides rose from 597 to 667 mg. per 100 ml. and the associated acidosis necessitated cessation of resodec treatment. Resumption of low sodium diet reduced the sodium intake by at least 75 per cent, but sodium excretion only fell 25 per cent so that negative sodium balance persisted.

These results lend support to the view that the kidney in congestive failure is unable to maintain sodium balance when the sodium intake exceeds a certain critical level—in this patient between 70 and 105 m-eq. (1600 and 2400 mg.) per day. Although the kidney is capable of achieving a vastly higher output of sodium per day (as seen during the last 3 days of resodec administration), the excretion does not rise proportionately to the intake, and negative balance can only be obtained when the intake is cut down.

Side-effects

Undesirable side-effects appeared in half the cases.

Hyperchloræmia occurred on three occasions, twice in one patient accompanied by mild dyspepsia and gastric acidity, once in another case when it caused more severe dyspepsia, anorexia, irritability, depression and a serious fall in CO_2 combining power of the blood. The former patient was having resodec in addition to low sodium diet and was still receiving supplementary ammonium chloride which probably accounts for her acidosis. The other patient was on ward diet without supplementary ammonium chloride; he had defective renal function.

TABLE III

SODIUM INTAKE, URINARY SODIUM EXCRETION, SERUM SODIUM AND WEIGHT IN CASE 1 ON DIFFERING REGIMES

Period	Regime	Sodium intake (m-equiv./day)	Urinary sodium (m-equiv./day)	Serum sodium mg./100 ml.)	Weight in kg.
Dec. 1 to 5	Low sodium diet No extra chloride	35	56	340	64·3→65·2
Dec. 10 to 18	Low sodium diet + 3 drams HCl	35	74	337 330	63·9→64·8
Dec. 19 to 25	Low sodium diet + 2 grams NaCl	70	110	344	64·8→66·6
Dec. 26 to Jan. 4	Low sodium diet + 3 grams NaCl	105	100	336	66·6→66·5
Jan. 5 to 9	Low sodium diet + 4 grams NaCl	140	119		66·1→67·0
Jan. 10 to 12	Ward diet Salt *ad lib*	Over 140	147		66·6→68·0
Jan. 13	Ward diet, salt *ad lib* + Resodec 45 grams	Over 140	113		68·4
Jan. 14 to 16	do.	Over 140	142		68·4→68·0
Jan. 17 to 19	do.	Over 140	193	344	68·0→66·6
Jan. 20 to 22	do.	Over 140	211		66·6→63·9
Jan. 23 to 25	Low sodium diet No extra chloride	35	153	366	63·9→64·3

Hyperkalæmia developed in two patients. One with a serum potassium level of 26 mg. per 100 ml. had mild diarrhœa, vague abdominal discomfort, irritability and petulance; she refused to continue treatment. In the second case a serum potassium level of 38, rising later to 40 mg. per 100 ml. was accompanied by transient diarrhœa, nausea, vomiting and hyponatræmia. Both these patients had previously been on low sodium diet but were having ward diet during resin administration.

Hypokalæmia occurred twice. One patient who was on low sodium diet plus resodec and whose serum potassium was 17·4 mg. per 100 ml. on the first day of treatment, became sick, weak, mentally confused, and incontinent of urine. A symptomless hypokalæmia with 15·4 mg. potassium per 100 ml. was found in the second patient after 8 days' treatment with resodec and ward diet.

Digitalis intoxication appeared in one patient, an occurrence noted also by previous authors.

Finally, one patient became delirious when originally rendered œdema-free by low sodium diet, and delirium recurred when treated by resodec for return of œdema; the delirium could not be correlated with any biochemical change and was attributed to left heart failure. Apart from the more serious side-effects of the resin, most of our patients have complained that it leaves a lingering sticky feeling on their lips, tongue, and palate; and many of them have preferred the dietetic regime to the resin.

SUMMARY AND CONCLUSIONS

The effects of " resodec " (a balanced ammonium-potassium carboxylic resin) on 10 patients with congestive heart failure have been studied clinically and biochemically during fourteen courses of treatment.

The resin produces clinical results similar to those of dietetic sodium restriction but sometimes

with undesirable side-effects which are in the main due to hyperchloræmia or to development of abnormal serum potassium levels.

Biochemical control is essential in the early stages of treatment. This is especially important in patients with renal impairment and in those who have been on sodium restricted diet or on mercurial diuretics; such patients may have abnormal blood electrolyte levels resulting from previous treatment. These abnormalities are sometimes corrected but sometimes aggravated by resin therapy.

Subject to biochemical control, the resin can be used as a substitute for low sodium diet or in conjunction with the diet to reinforce the latter. When given in addition to low sodium diet, the best result was obtained with repeated short courses. Ammonium chloride should be discontinued during periods of resin administration.

The wide variations in the behaviour of serum potassium during resin administration suggest the desirability of having two or more resins with differing potassium contents, suitable for administration either with a rising or a falling serum potassium level; it is hoped to investigate this possibility when suitable patients present themselves.

Low sodium diet tends to produce hypochloræmia: resin therapy tends towards hyperchloræmia. Patients intolerant to one of these forms of treatment may prove ideal for the other.

Our especial thanks are due to Messrs Smith, Kline, and French for ample supplies of resodec: to Dr. Ian Anderson and his staff of the Biochemical Laboratory for their numerous and painstaking estimations of blood and urinary electrolytes and for analysis of diets; to Drs. J. J. McCall, C. McNaughton, A. K. Bain, and R. I. Alexander, Registrar and Resident House Physicians for their general help and supervision of patients; and to Sisters Fraser, Coats, and Harrower for their co-operation throughout the investigations.

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CASE REPORTS

A-V DISSOCIATION IN DYSTROPHIA MYOTONICA

BY

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Disturbance of cardiac rhythm in association with dystrophia myotonica has been recognized since Griffith (1911) recorded his finding of bradycardia in a patient with this disease. Since then other cases have been described and the subject has been reviewed by Spillane (1951) and Fisch (1951), the latter author concluding that of 85 cases of dystrophia myotonica 68 per cent had abnormal electrocardiograms and that of these 91 per cent were conduction defects and/or disturbances of rhythm.

The degree of cardiac involvement is generally slight but the case here reported was probably unique in presenting with Stokes-Adams attacks and terminating fatally.

Clinical Description

In 1941 Mrs. A. W., then aged 42 years, had an attack of unconsciousness of short duration. During the ensuing nine years further attacks of varying severity occurred at irregular intervals. There were no further symptoms of cardiovascular or other disease and no previous history of rheumatism or serious illness. The patient had never been pregnant.

An electrocardiogram in 1950 showed latent heart block (P–R., 0·28 sec.), and left bundle branch block. A diagnosis of Stokes-Adams attacks was made and treatment with atropin sulphate 1/100 of a grain by mouth four times daily was started. There was freedom from attacks for six weeks followed by their gradual return until in August 1951, their incidence was more frequent than ever and quite uninfluenced by atropin. She was admitted to hospital in February, 1952, and on the same day a typical Stokes-Adams attack was witnessed.

Examination of the cardiovascular system showed no signs of congestive failure. Peripheral arteries were clinically normal, pulse regular, rate 42, blood pressure 140/65. The heart was not enlarged, the cardiac impulse normal; the first heart sound was occasionally augmented, presumably by the auricular sound. The second heart sound was widely split in all areas. No murmurs were audible.

The facies was myopathic and bilateral ptosis was present; the speech was slurred and monotonous. There was muscular wasting, severe in the sterno-mastoid, spinati, and trapezii, and moderate in the muscles of the upper arms and thighs and associated with appropriate weakness. The grip was myotonic, the tendon reflexes diminished generally, and the thyroid gland diffusely enlarged.

Serum Wassermann and Kahn reactions were negative and lumbar puncture normal; slight left ventricular enlargement was demonstrated by teleradiogram. Gastrocnemius muscle biopsy showed considerable interstitial accummulation of adipose tissue cells which separated the bundles of muscle fibres. The latter showed considerable variation in size, and many were atrophic; a very small proportion of hypertrophied fibres were present. In a few muscle fibres were rows of centrally placed nuclei. Neither striated annulets nor excess of sarcoplasm was seen in relation to any muscle fibre. The appearances corresponded with those described by Wohlfart (1951), although not all the features that he mentioned were present.

Electrocardiograms showed varying degrees of A-V conduction from sinus bradycardia (Fig. 1 A), to complete A-V dissociation (Fig. 1B). The shape of the ventricular complexes varied, being at all times abnormal and changing indiscriminately from the appearances of left bundle branch block to those of right bundle branch block (Fig. 1C). Stokes-Adams attacks continued to occur frequently while the patient was in hospital and a cardiogram made during one such episode showed probable ventricular tachycardia which, on recovery, was followed by complete A-V dissociation (Fig. 1D).

In an attempt to control the incidence of ventricular tachycardia it was decided that a course of quinidine sulphate should be given. The test dose of 3 grains was followed by such severe tinnitus and increased

frequency of syncopal attacks that use of the drug was abandoned. On March 20, treatment with ephedrine hydrochloride, ¼ of a grain t.i.d. was started and immediately the syncopal attacks stopped. At the end of April they reappeared and in one of them at home the patient died. We have ascertained that she had stopped taking ephedrine. No post-mortem examination of the body was made.

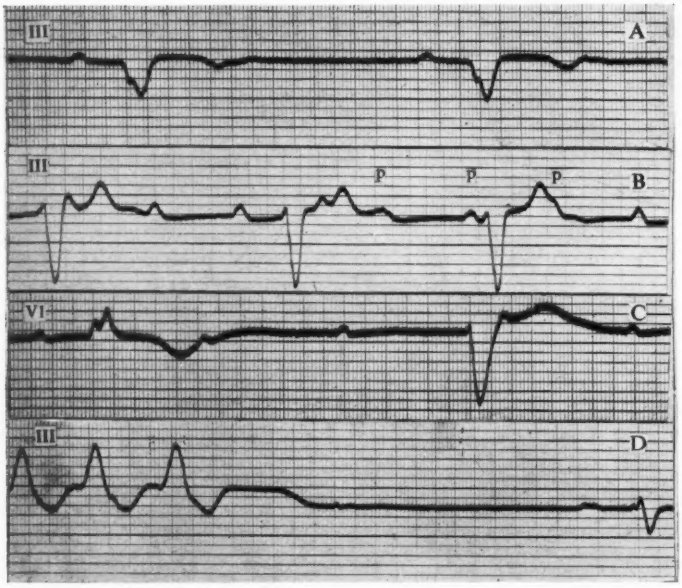

FIG. 1.—(A) Sinus bradycardia at 36 a minute. P–R, 0·26 sec., and left bundle branch block. (B) Complete A-V dissociation, auricular rate 133, ventricular rate 46; auricular rhythm not quite regular. (C) Complete A-V dissociation; ventricular complexes of varying type. (D) Electrocardiogram taken toward the end of a Stokes-Adams attack showing ventricular tachycardia, rate 170, followed by complete A-V dissociation.

Discussion

Although the main impact of dystrophia myotonica is usually upon skeletal muscles, in the case described the symptoms pointed to early severe heart involvement; only much later were there any complaints referable to the neuro-muscular system. It might be argued that the patient's preoccupation with the syncopal attacks explain why the comparatively minor disabilities of motor weakness and myotonia were overlooked. On the other hand, the disease may exist in the absence of symptoms, as was demonstrated by the patient's brother who, although declaring himself to be well and strong, had signs of advanced dystrophia myotonica.

Reports of such severe cardiac damage as was seen in this case are few. Brain (1951) mentions the occurrence of complete heart block and one case from a series reported by Evans (1944) had two probable Stokes-Adams attacks, a long P–R interval (0·30 sec.), and atypical bundle branch block. Broustet (1945) describes auricular flutter with A-V dissociation in the presence of an atypical myopathy; the significance of the association in this case is doubtful, however, as the patient had hypertension.

Although in our case disturbance of A-V conduction is undeniable, caution must be exercised in interpreting the abnormal QRS complexes as evidence of one or other type of bundle branch block. It is more likely that the variation in complexes indicated the establishment of ectopic foci of stimulation in one or other ventricle. The labile nature of the cardiographic changes in this case may, perhaps, indicate that errors of cardiac conduction in dystrophia myotonica represent functional change rather than severe myocardial disorganization.

Summary

A case of dystrophia myotonica in which Stokes-Adams attacks were early manifestations of the condition is described. The attacks were due to the onset of abnormal ventricular rhythm in the course of A-V dissociation. The absence of other causes of cardiac disease enhances the probability that the heart block was related to the dystrophy, the heart lesion being of unusual severity.

I wish to thank Dr. W. C. Smallwood for his helpful criticism and Dr. W. St. C. Symmers for his report on the muscle biopsy.

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EBSTEIN'S ANOMALY DIAGNOSED DURING LIFE

BY

C. B. HENDERSON, FREDERIC JACKSON, AND W. G. A. SWAN

From the Regional Cardiovascular Department, Newcastle General Hospital

The downward displacement into the right ventricle of a deformed tricuspid valve is the characteristic feature of Ebstein's anomaly. There is a large proximal cavity composed of the right atrium and part of the right ventricle and a distal cavity formed by the rest of the right ventricle. There is usually a large defect of the atrial septum. The association of the lesion with cardiac arrhythmia and bundle branch block has been stressed by Taussig (1947) and Brown (1950). Engle *et al.* (1950) reviewed the reported cases and, with three of their own, brought the total number to 26 at that time. None had been diagnosed before death. Baker *et al.* (1950) reported two cases with necropsy control in one of which crural embolism followed cardiac catheterization. Reynolds (1950) published the first report of a case diagnosed during life; angiocardiography and cardiac catheterization showed evidence of a very large right atrium and a defect of the atrial septum. Soloff *et al.* (1951) also made the diagnosis in life mainly on angiocardiographic evidence. van Lingen *et al.* (1952) described two further cases in which the diagnosis was suggested by catheter findings.

Case Report

A man, aged 26, was found to have an abnormal heart at the age of four and on medical advice he led a restricted life, avoiding strenuous exertion, but was able to work as a mining engineer. Two days before admission he felt rapid palpitation after cycling and his breathing became distressed. On admission he was noted to be a well-built man. He was dyspnœic and cyanosed at rest, but there was no clubbing of the fingers. The apex rate was 110 a minute and the rhythm was auricular fibrillation. The blood pressure was 110/75; the jugular veins were distended to a height of 4 cm. above the sternal angle in the erect posture. There was no other clinical evidence of heart failure. The apex beat was in the sixth interspace outside the mid-clavicular line. There was no thrill. The first heart sound was split at the apex, and the second sound at the left border of the sternum was split but not exceptionally loud. A very soft early diastolic murmur was later heard to the left of the sternum. A blood count showed 7,410,000 red cells per c.mm. and hæmoglobin 17·8 g. per 100 ml.

Radioscopy on admission showed a very large heart with apparent marked enlargement of the right atrium and right ventricle and slight enlargement of the left atrium but no dilatation of the pulmonary artery; there was pulmonary congestion but no hilar dance. The heart rate slowed in response to digitalis. Next day the apex rate was 80 a minute and the lungs were free from radiological signs of congestion (Fig. 1).

The electrocardiogram showed auricular fibrillation and right bundle branch block. Regular rhythm returned two days after cardiac catheterization and has since been maintained; the bundle branch block persists (Fig. 3).

Atrial septal defect was first suspected but the absence of enlargement of the pulmonary artery and of a hilar dance with such a large heart were against this diagnosis (Bedford *et al.*, 1941).

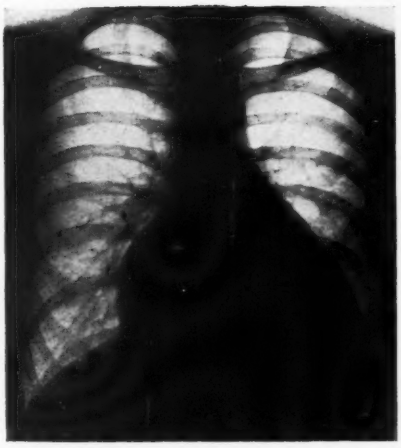


FIG. 1.—Teleradiogram, showing a large heart with prominent right atrium, but with no obvious enlargement of the pulmonary trunk and its branches.

FIG. 2.—Film showing the catheter looped in the outflow portion of the right ventricle.

Cardiac catheterization was carried out. The catheter tip passed easily into the right ventricle and pulmonary artery describing a wide arc along the periphery of the cardiac shadow. The transition from atrial to ventricular pulsation occurred midway between the right and left borders of the heart, accompanied by only a slight rise in the mean pressure. The catheter could be made to loop in the upper part of the right ventricle in an unusual manner, and as the tip descended it met an obstruction at the same point each time (Fig. 2); pressure readings and blood samples confirmed that it was still in the ventricle. The impression gained was of an enormous right atrium and ventricle and of an outflow chamber in which the arrest of the catheter tip seemed compatible with a displaced tricuspid leaflet.

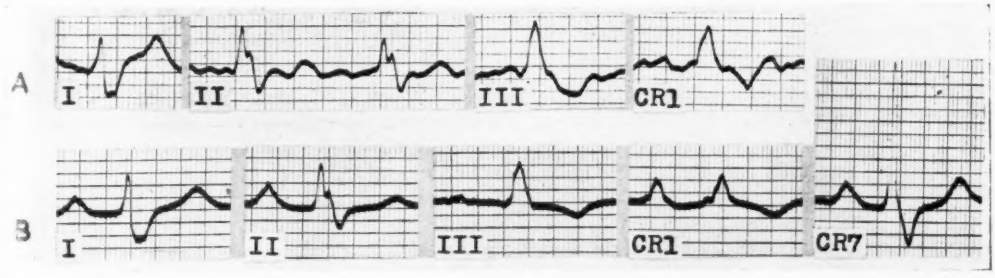
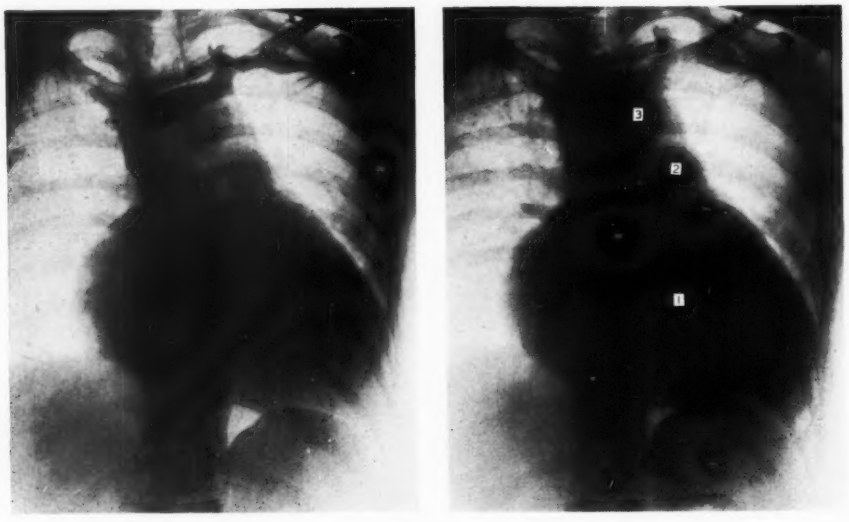


FIG. 3.—Electrocardiograms showing right bundle branch block. (A) Auricular fibrillation. (B) Normal rhythm (see text).

Site	Mean pressure in mm.Hg. relative to right atrium	Percentage oxygen saturation
Superior vena cava	7·5	60
Right atrium	7	68
Right ventricle	9–10	68
Main pulmonary artery	14	69
Femoral artery	—	91

An *angiocardiogram* showed a very large right atrium two seconds after injection (Fig. 4A). One second later the whole heart shadow was opacified and the contrast medium was present in both pulmonary artery and aorta (Fig. 4B). There was poor filling of the pulmonary vessels and some opacification of the heart was still seen up to ten seconds.



A B

FIG. 4.—Angiocardiogram. (A) Two seconds after injection. Large right atrium outlined. (B) Three seconds after injection. Whole heart opacified (1), simultaneous filling of pulmonary artery (2) and of aorta (3).

Summary

The diagnosis of Ebstein's malformation with atrial septal defect seems probable in this case on the following grounds.

(1) A very large heart with particular enlargement of the right atrium and right ventricle without enlargement of the pulmonary artery and its branches in a patient with congenital heart disease who shows only slight cyanosis and early cardiac disability at 26 years.

(2) Cardiac arrhythmia and right bundle branch block.

(3) Low pressures on the right side of the heart with a very small pressure gradient between the atrium and the ventricle.

(4) Great enlargement of both right atrium and ventricle, including the outflow portion, shown by catheterization and the angiocardiogram.

(5) Suggestive evidence of displacement of the tricuspid valve.

(6) A large atrial septal defect with a shunt in both directions.

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Editorial Note

Dr. Paul Wood informs me that among the patients he has diagnosed as Ebstein's disease, four or five have had catheterization and one died suddenly during this. At Guy's Hospital I have made the diagnosis in ten cases, two of whom were acyanotic and the others cyanotic. Six of these have had catheterization and one died, almost certainly as the result of intracardiac thrombosis.

We have heard of other deaths and complications arising after catheterization in cases of Ebstein's disease, and think that as the diagnosis can often be made on clinical grounds catheterization should not be carried out unless there are very special reasons for it.

MAURICE CAMPBELL

ABSTRACTS OF CARDIOLOGY

Edited by Dr. J. L. Lovibond in collaboration with Abstracts of World Medicine

Peripheral Aneurysm and Arteriovenous Fistula. S. M. COHEN. *Ann. Roy. Coll. Surg. Engl.*, **11**, 1–30, July, 1952.

His experience in a centre for vascular diseases during the last war is the basis of this article, in which the author suggests an explanation of behaviour of the circulation in aneurysm and arterio-venous fistula. Pulsatile stretching is the stimulus for the production of elastic tissue; the thickening of a vein grafted into an artery, or of one taking part in an arterio-venous fistula are examples of this process. Contrariwise, the thinned, dilated afferent arterial trunk to such a fistula undergoes these alterations because of the loss of pulse pressure resulting from the fistula. The number and tortuosity of the collateral channels that develop after occlusion of a main artery depend upon the peripheral resistance in the distal segment. If this is healthy, resistance is low and the by-passing vessels are short and direct; they share with the normal artery, which they bridge, a pulsatile content. If pulsation be restored to the dilated artery leading to a fistula by ligation, shortening and reduction in diameter follow. Post-stenotic aneurysms are due to loss of the normal impulse beyond the obstruction.

C. G. Rob

Anæsthesia and the Cardiac Patient. G. W. HAYWARD. *Anæsthesia*, **7**, 67–71, April, 1952.

The author assesses the operative risks of major surgery in patients with heart disease as being only a little higher than in those without heart disease provided full advantage is taken of up-to-date surgical and anæsthetic techniques. He regards two factors as of especial importance—anoxia and hypotension. He considers that sudden death is most likely to occur in patients with coronary disease, aortic stenosis, syphilitic aortitis, heart-block, or a large patent ductus arteriosus; "death is usually the result of ventricular fibrillation in these patients." Preoperative treatment with procaine amide hydrochloride (pronestyl) is advised in a dosage of 500 to 1000 mg. orally; if cardiac irregularity occurs during operation the drug may be given intravenously at a rate not exceeding 100 mg. per minute up to a total dose of 1000 mg.

It is pointed out that controlled hypotension is regarded by cardiologists as particularly dangerous in elderly arteriosclerotic patients or in those with coronary disease, but that too little is known about the effects of this technique for a balanced opinion to be given. It is stated that whereas hypotension can be avoided in those with a history of angina pectoris or other suggestive signs of coronary impairment, it is not uncommon for coronary insufficiency to be silent until myocardial ischæmia occurs during operation, and there is no reliable way of detecting it pre-operatively. In view of such unpredictable risks it would therefore seem wise at present to restrict the use of controlled hypotension to operations where success depends on a bloodless operative field, thus justifying acceptance of the increased risks involved.

It is recommended that in congestive heart failure operation be postponed until the heart rate has been stabilized, and pulmonary congestion should be counteracted by careful control over the fluid balance and the use of mercurial diuretics. As the author says, "one method of treating or preventing attacks of acute pulmonary œdema in man is the administration of a rapidly acting barbiturate."

Cardiac arrhythmias are not considered to call for specific measures beyond normal care; and it is suggested that angiocardiography is best performed under basal narcosis in adults, but under general anæsthesia in children.

[The author is to be congratulated on a very concise review of the subject which is a valuable and practical contribution.] *Michael Kerr*

Prognosis of Angina Pectoris. Observations in 6882 Cases. W. J. BLOCK, E. L. CRUMPACKER, T. J. DRY, and R. P. GAGE. *J. Amer. med. Ass.*, **150**, 259–264, Sept. 27, 1952.

The case histories of 6882 patients suffering from angina pectoris associated with coronary sclerosis who were examined at the Mayo Clinic over a period of 18 years have been analysed. The minimum follow-up period was 5 years and the maximum 23 years.

The average age at diagnosis in the Clinic was 58·8 years, at which time the average duration of the angina was 2·5 years. Mortality was greatest in the first year (about 15%) and was about 9% annually thereafter. The 5-year survival rate for the entire series was 58·4%, compared with 86·9% for the normal population. The 10-year survival rate was 37·1%, compared with the normal rate of 70·4%. Patients in the younger age groups showed higher survival rates at the 5- and 10-year periods than the older patients, but in each group the rate bore about the same relation to the normal. The prognosis was better in women, with a 10-year survival rate of 49%, than in men.

The presence of cardiac enlargement, hypertension, myocardial infarction, and congestive failure influenced the prognosis unfavourably. Electrocardiographic findings were of definite prognostic value. Thus the 10-year survival rate for patients with normal tracings when first seen was 50%, for those with Q- or T-wave changes in

the electrocardiogram 24%, for those with evidence of left bundle-branch block 14%, and for those with auricular fibrillation 13·5%. The 10-year survival rate for patients in whom angina was associated with obesity or gall-bladder disease was 44%, with thyroid disease 37%, with diabetes 21%, and with carcinoma 17%. The reason for the more favourable outlook in the first group is not clear.

T. Semple

An Evaluation of Anticoagulant Therapy in the Treatment of Acute Myocardial Infarction. H. I. RUSSEK and B. L. ZOHMAN. *Amer. Heart J.*, **43**, 871–880, June, 1952.

At the State University of New York College of Medicine 1047 patients suffering from myocardial infarct were examined and classified as " good " or " bad " risks on the day of admission to hospital; in 60% of cases admission took place within 24 hours of the attack. All those revealing a previous myocardial infarct, intractable pain, persistent or severe shock, enlarged heart, congestive failure, gallop rhythm, fibrillation, flutter, tachycardia or block, varices, and diabetic acidosis were classified as bad risks. Conservative treatment without the use of anticoagulants was instituted. The crude mortality rate was 33%, 3% in the former group and 60% in the latter. Similarly the incidence of thrombo-embolic complications in the survivors was 0·8% in the " good " group and 10% in the " bad " group. It is concluded that the use of anticoagulants is not justified in " good risk " cases of infarct, especially as most of the cases that died in this group could not have been affected by such treatment, as death was not primarily due to thrombosis.

No correlation was found between age and prognosis; the division into two groups as a result of clinical findings was all-important in prognosis. It follows, therefore, that the decision as to whether or not anti-coagulants are used depends on the findings in the individual case, only the " bad risks " being given this treatment. The replies to a questionary issued to American consultant physicians indicated that about one-half of them use anticoagulants routinely, partly as a result of pressure from patients or their relatives, and from practitioners. Not unexpectedly, some 45% of the consultants had encountered serious hæmorrhagic complications. The routine use of anticoagulant therapy is deprecated by the authors.

James D. P. Graham

Factors Influencing Rupture of the Heart After Myocardial Infarction. R. W. OBLATH, D. C. LEVINSON, and G. C. GRIFFITH. *J. Amer. med. Ass.*, **149**, 1276–1281, Aug. 2, 1952.

The authors review the records of 80 cases of perforation of the heart following myocardial infarction which have occurred at the Los Angeles County Hospital in the last 10 years. From this study he following points emerge: the mean age incidence was about 70 years, none of the patients being under 50; slightly more than half the patients were women; cardiac rupture occurred in 7% of all hospital cases of myocardial infarctions.

The complication seemed to be unrelated to the interval elapsing before the institution of treatment, for four-fifths of the cases were admitted within 72 hours of onset. There was no evidence that ordinary activity predisposed to rupture. In about half the cases rupture occurred within 72 hours and in 14 cases in less than 24 hours; in 6 cases intervals of from 19 to 30 days were noted. A QS pattern in the electrocardiogram was often seen and in the opinion of the authors would have been found in all cases had sufficient leads been taken. Persistent hypertension after infarction was the rule. No evidence was found to incriminate digitalis or other drugs.

At necropsy the striking feature was the close relationship of the site of perforation to the interventricular septum, being in, parallel to, or adjacent to that structure in 67% of cases. The great majority of perforations were dissections by devious routes from the endocardium to the pericardium; direct rupture was rare.

H. David Friedberg

The Routine Use of Quinidine in Acute Myocardial Infarction. F. B. CUTTS and B. RAPOPORT. *New. Engl. J. Med.*, **247**, 81–83, July 17, 1952.

The authors studied the effect of quinidine on the incidence of arrhythmia and of sudden, unexpected death in cases of myocardial infarction treated with dicoumarol. The patients, in all of whom there was clear electrocardiographic evidence of recent infarction, were divided into 3 groups. In the first group 66 patients received 0·2 g. of quinidine orally 4 times a day; in the second group 20 patients received 0·4 g. every 8 hours; in the third group 25 patients received 0·6 g. every 8 hours. Controls numbered 55 in the first group, 20 in the second, and 25 in the third.

The incidence of extrasystoles was the same in all groups. Auricular fibrillation and flutter occurred in some cases in each group; the beneficial effect of quinidine in preventing these irregularities was difficult to prove and, at best, was only moderate. There was no evidence that quinidine either prevented or promoted auriculoventricular block. No significant difference in mortality between the groups was noted. The incidence of sudden death (excluding death from myocardial rupture) was least in the group receiving 0·2-g. doses, and it is suggested that the heavier dosage may have been responsible for some of the deaths. It is concluded that there is no indication for the routine use of quinidine in acute myocardial infarction. *R. S. Stevens*

The Reversibility of Malignant Hypertension. G. W. PICKERING, A. DICKSON WRIGHT, and R. H. HEPTINSTALL. *Lancet*, **2**, 952–956, Nov. 15, 1952.

Essential hypertension behaves in one of two ways: in the majority of patients it pursues a relatively benign course over many years, to terminate in heart failure, apoplexy, or intercurrent disease; in a few patients, usually younger, it follows a rapidly fatal course, with albuminuric retinitis and progressive renal failure terminating in uræmia. It has been suggested that this latter malignant type is an expression of the severity of the hypertensive process and occurs if the arterial pressure

rises and is maintained above a certain critical level so that arteriolar necroses occur; and further, that if this sustained pressure can be reduced sufficiently and for long enough the malignant form of the disease should revert to the benign form.

The present authors describe the clinical findings in 3 cases of malignant hypertension, with arteriolar necroses in the kidney and adrenal glands, and albuminuric retinitis. Arterial pressure was reduced by nephrectomy in one patient, by subtotal adrenalectomy in the second, and by sympathectomy and subtotal adrenalectomy in the third. As a result the 3 patients remain alive and well 5 years after operation, with less severe hypertension normal blood urea level, and normal urea concentration.

It is concluded that malignant hypertension is reversible, and that the benign and malignant forms are the simple consequences of the severity of the hypertension.

James W .Brown

Prolongation of Action of Hypotensive Drugs. Use of Polyvinylpyrrolidone and Dextrans to Lengthen Effects of Hexamethonium and Hexamethylene Bisethyldimethylammonium. F. H. SMIRK. *Lancet*, **2**, 695–699, Oct. 11, 1952.

By incorporating either poly-vinyl-pyrrolidone or dextran in the solution for subcutaneous injection of methonium drugs absorption of the latter is delayed and their hypotensive action is prolonged. The duration of their action can be further prolonged, so that they become significantly effective for a full 5 to 8 hours, by the addition of a local vasoconstrictor such as ephedrine hydrochloride. It is usually necessary to increase the dose of the methonium compound by at least 30% when changing from a simple aqueous solution to the slowly-absorbed preparation. Oral administration of hexamethonium bromide is useful when the blood pressure begins to rise again after injection of the slow-absorption preparation, steady control being possible by this method equivalent to three subcutaneous injections of the simple aqueous solution.

J. L. Lovibond

High Blood Pressure in the Elderly. H. DROLLER, J. PEMBERTON, C. ROSEMAN, and J. L. A. GROUT. *Brit. med. J.*, **2**, 968–970, Nov. 1, 1952.

From a random sample, taken from the Sheffield food office register, of people of pensionable age, a group of 476, who were living at home, either alone or alone with spouse, were medically examined, and the incidence among them of arterial hypertension, with reference to its association with other signs and symptoms, was analysed. It was found that 57% of the men and 77% of the women had a systolic pressure of 160 mm. Hg or more, and 28% and 48% respectively had a diastolic pressure of 100 mm. Hg or more. No case of malignant hypertension was found, all the cases of hypertension being regarded as benign. The difference in blood pressure between certain age groups was not significant.

The presence of vertigo or of tinnitus could not be related to the blood pressure level, nor could the presence of angina of effort be related to the degree of hypertension. The incidence of arteriosclerosis increased significantly with age, but the degree of arteriosclerosis was not related to the degree of hypertension. Arteriosclerosis was, in fact, commoner in men than women, while hypertension was commoner in women. There was no significant association between the blood pressure level and the size of the heart, estimated from a chest radiograph.

J. C. Brocklehurst

Commissurotomy for Mitral Stenosis (Results and Indications for Operation). P. SOULIÉ, J. DI MATTÉO, R. TRICOT, and L. MOREAU. *Bull. Soc. méd. Hôp. Paris*, **68**, 871–894, 1952.

Since September, 1950, the authors have performed mitral valvotomy in 52 out of 55 cases operated upon; there were 5 postoperative deaths, 3 of which occurred in long-standing advanced cases. Of the 52 patients, 35 have been followed up for 3 months or more, and of these about three-quarters were greatly improved by the operation, while in one-quarter there was little or no improvement.

The selection of patients and their investigations is described in detail. The authors affirm that the ideal indications for the operation are: an uncomplicated mitral stenosis occurring in a patient between 25 and 35 years of age, with marked functional difficulties (such as recurrent pulmonary œdema, dyspnœa on effort, and hæmoptysis), no notable enlargement of the heart volume, electrocardiographic signs of overloading of the right ventricle, increased pressure in the pulmonary circulation, and a diminution of the mitral surface to less than 1·5 sq. cm. The results of cardiac catheterization are of particular interest in those cases in which there is an unusually high gradient between pulmonary artery pressure and capillary pressure. This is apparently due to a raised pulmonary peripheral resistance other than the passive hypertension caused by the mitral stenosis. In keeping with these findings pulmonary atheromatous changes were found at necropsy in 3 of their cases.

S. F. Stephenson

The Diagnosis of Mitral Incompetence accompanying Mitral Stenosis. Review of Eleven Cases Treated Surgically. A. LOGAN and R. TURNER. *Lancet*, **2**, 593–598, Sept. 27, 1952.

The authors, working in Edinburgh, have studied 60 patients who have undergone a thoracotomy for mitral disease. They consider that the classical signs of mitral incompetence (apical systolic murmur; enlargement, often with systolic expansion, of the left atrium; and clinical, radiological, or electrocardiographic evidence of left ventricular hypertrophy) are not present in all cases. Even in the presence of a murmur of mitral stenosis, predominant incompetence should be suspected if the first heart sound at the apex is absent or faint and if the opening snap of the mitral valve is not heard. The left atrium is usually considerably enlarged if there is any significant incompetence. Systolic expansion of the left atrium is a reliable sign only if it is gross. "Systolic expansion" has been observed preoperatively in patients in whom no regurgitation has been felt at operation.

In these cases it is probable that the appearance of systolic expansion has been due to backward displacement of the whole atrium. The detection of hypertrophy or dilatation of the left ventricle is important in a patient with mitral stenosis, since it signifies some complicating lesion—usually systemic hypertension, aortic valvular disease, or mitral incompetence. If, as is usual, hypertension and aortic valvular disease can be excluded, even slight ventricular enlargement indicates mitral incompetence.

A series of 11 patients suffering from mitral incompetence have been treated surgically by placing a pedicled sheet of pericardium across the ventricular surface of the mitral valve. In 4 cases there was also a stenosis, requiring a preliminary valvulotomy. The breadth of the regurgitant stream felt on the intracardiac finger was generally more significant than its force. A 7-in. (17·5 cm.) silver probe was passed eye first through the ventricle from front to back, and then threaded with a sheet of pericardium pedicled on the diaphragm opposite the auriculo-ventricular ring. The probe was withdrawn, followed by the graft, which was then sutured to the ventricular wall. The position and tension of the graft were ascertained by palpation from within the atrium through the mitral valve. The point of entry of the probe was in the angle between the left coronary artery and its interventricular branch, 2 cm. from each vessel. The point of exit was similarly related to the left coronary artery and the interventricular branch of the right coronary artery.

Although 10 patients have been improved (3 to 10 months after operation), no final assessment of the value of the operation can yet be made. There have been no deaths. *R. L. Hurt*

The Left Auricular Pressure Pulse in Normals and in Mitral Valve Disease. A. WYNN, M. B. MATTHEWS, I. K. R. MCMILLAN, and R. DALEY. *Lancet*, **2**, 216–219, Aug. 2, 1952.

At St. Thomas's Hospital, London, the pressure in the left auricle was recorded during thoracotomy in 14 patients with normal rhythm, in 19 patients with mitral stenosis and normal rhythm, and in 18 patients with mitral stenosis and auricular fibrillation. In some patients the left auricular pulse was also recorded after valvotomy. In patients with normal hearts the first event is a wave due to auricular systole varying from 2 to 8 mm. Hg in amplitude; this is followed rapidly by a further rise in pressure beginning at the end of the QRS complex, but this deflection may be slight or absent. There is then a marked fall in auricular pressure followed by a rise reaching its peak (1 to 9 mm. Hg) 0·04 to 0·12 second after the end of the T wave. Then follows a sharp fall in pressure at the opening of the mitral valve, which is followed by a slight rise before the next auricular systole.

In a few patients tracings were obtained from the right auricle and these were similar in form to those from the left. In 5 patients with mitral stenosis significant mitral incompetence was found at operation. There was no striking difference in tracings of the left auricular pressure in these patients from those from patients with no mitral incompetence. But in one patient with preoperative mitral incompetence the pressure in late systole rose to 25 mm. Hg. It is concluded that mitral regurgitation in the presence of mitral stenosis does not produce a qualitative change in the form of the left auricular pressure tracing. *C. Bruce Perry*

The Role of the Bronchial Veins in Mitral Stenosis. J. C. GILROY, P. MARCHAND, and V. H. WILSON. *Lancet*, **2**, 957–959, Nov. 15, 1952.

Two distinct systems of bronchial veins may be distinguished: (1) the true bronchial veins, which drain the intrapulmonary bronchi and the interstitial framework of the lung; and (2) the pleurohilar veins, which drain the hilar structures and the subpleural planes of the lung. The true bronchial veins drain into the pulmonary veins, whereas the pleurohilar veins empty into systemic veins, such as the azygos or intercostal veins. The pleurohilar veins communicate freely with the pulmonary veins at the hilum and in the subpleural plane.

Necropsy in 6 cases of mitral stenosis revealed congestion and dilatation of the pleurohilar veins, which were shown to communicate freely with the pulmonary veins and drained directly into the azygos and hemiazygos veins. These findings conform with the observation of grossly congested hilar veins at operation. Dilitation of the pleurohilar veins suggests a mechanism whereby the rise in pressure in the pulmonary veins may be modified and considerable amounts of blood take part in a circus movement through them from the right ventricle to the right auricle without traversing the left side of the heart. It is suggested that the " stiff lung " of mitral stenosis is explained by a rise in bronchial venous pressure, which may ultimately cause a transudation of œdema fluid into the supporting interstitial framework of the lung, thus causing rigidity without any intra-alveolar pulmonary œdema.

James W. Brown

The Relapsing Form of Acute Benign Pericarditis of Unknown Ætiology. B. COBLENTZ, J. L. FUNCK-BRENTANO, and J. LENÈGRE. *Sem. Hóp. Paris*, **28**, 2923–2931, Oct. 2, 1952.

The authors describe 3 cases of pericarditis in which the disease lasted about 6 weeks but relapsed from 3 to 5 times over the course of the next 6 months. No definite ætiology could be determined in these patients, whose ages ranged from 33 to 46 years. The literature of acute benign pericarditis is reviewed and from this it is noted that relapses occurred in 15% of the cases.

G. S. Crockett

Epidemic Non-specific Pericarditis. S. AAGAARD and S. E. JENSEN. *Nord. Med.*, **48**, 1409–1411, Oct. 10, 1952.

From the Central Hospital, Randers, Denmark, 7 cases of acute non-specific pericarditis are described. The age of the patients ranged from 11 to 36 years. The febrile period lasted for 3 to 21 days, and pericardial friction

was observed for periods up to 17 days. There were no signs of cardiac inefficiency, but a shock-like condition with tachycardia and hypotension was seen in some patients. Rheumatic fever was excluded in all cases. The patients were treated with ACTH, 40 mg. daily for 10 days; some subjective improvement was noted. Five of the cases occurred during an epidemic of Bornholm disease, and it is suggested that the two conditions may be associated. *D. J. Bauer*

Lesions in Auricular Appendages Removed at Operations for Mitral Stenosis of Presumed Rheumatic Origin. D. C. SABISTON and R. H. FOLLIS. *Bull. Johns Hopk. Hosp.*, **91**, 178–182, Sept., 1952.

The authors' description of the histological changes in the left auricular appendage removed at operation for mitral commissurotomy is based on 43 specimens removed by Blalock from patients with "pure" mitral stenosis, the ages of the patients ranging from 21 to 48 years. These histological changes are classified and illustrated. Rheumatic lesions are defined as Aschoff bodies or cellular accumulations leading thereto. The frequency and extent of the rheumatic lesions were not related to a history of rheumatic fever, or to the presence of fibrillation, or to age. There was some correlation with sedimentation rate, since all those with a raised sedimentation rate had rheumatic lesions.

E. G. L. Bywaters

Significance of Pulmonary Hypertension in Constrictive Pericarditis. A Pre- and Post-operative Study. J. G. SCANNELL, G. S. MYERS, and A. L. FRIEDLICH. *Surgery*, **32**, 184–189, Aug., 1952.

Cardiac catheterization was carried out before and after operation in 5 cases in which pulmonary hypertension was a constant feature of constrictive pericarditis. The authors found that there was no obstruction to the entrance of blood into the right auricle, but there was absence of filling of the ventricle during diastole. They noted a persistent rise in the pulmonary artery pressure and considered that the right and left sides of the heart were equally affected by the disease process. After operation the pulmonary arterial pressure remained significantly raised in 3 of the 5 patients, and in one it actually rose, although in all the pressure in the right side of the heart fell.

The importance of the release of both the left and the right ventricles at operation is emphasized.

J. R. Belcher

Surgical Closure of Defects of the Interauricular Septum by the Use of an Atrial Well. R. F. GROSS, A. A. POMERANZ, E. WATKINS, and E. I. GOLDSMITH. *New Engl. J. Med.*, **247**, 455–460, Sept. 25, 1952.

The authors have investigated the problem of the treatment of intra-atrial septal defects. They discuss the various methods by which attempts have been made to treat this lesion, and find them all open to criticism.

By means of extensive experiments on dogs they have developed a technique that employs an "atrial well," that is, a conical rubber funnel which is sewn to the atrial wall, and into which blood is allowed to flow from the open heart chamber until it reaches the level of mean intra-atrial pressure. Through the orifice at the lower end it has been possible to undertake deliberate intracardiac manœuvres without thrombosis in the well or interference with the circulation. Various methods for occluding the defect were tried, and are described. The authors have decided that where an orifice is 1 cm. or less in diameter it can safely be sutured, but where it is larger than this a plastic sheet should be sutured into place.

Using this technique the authors have now operated on 6 patients with intra-atrial septal defects. For use in human subjects they used a "well" 15 cm. in length with an upper orifice diameter of 13 cm., and a lower orifice diameter of 4 cm., capable of being expanded to 6 cm. by a special self-retaining retractor. Details of the cardiac lesion in the 6 cases are given. The first 4 patients died, but the last 2 survived and were very much improved, and it is felt that the operation may, in future, carry a low mortality. *J. R. Belcher*

Pericardial Cysts. W. M. LOEHR. *Amer. J. Roentgenol*, **68**, 584–609, Oct., 1952.

In this long article the author correlates previous reports on pericardial cysts, presents a classification, discusses the radiological aspects, and reports on 6 personal cases. The pathology of the various types is also described.

In discussing radiological diagnosis the author lays stress on fluoroscopic examination and spot films, and particular attention should be paid to alteration in size of the opacity with change in posture. The differential diagnosis is discussed; although certain features are helpful, diagnosis is still rather uncertain, and the decision as to whether operation is justified may be a difficult one. *Sidney J. Hinds*

Influence of Penta-erythritol Tetranitrate (Peritrate) on Acute and Chronic Coronary Insufficiency. T. WINSOR and P. HUMPHREYS. *Angiology*, **3**, 1–15, Feb., 1952.

Penta-erythritol tetranitrate, a white crystalline drug, was administered orally in doses of 1 to 6 10-mg. tablets daily to 125 patients with angina pectoris and an equal number with other forms of chest pain.

The patients recorded the number of attacks daily for 3 months while taking the tablets and for 3 months without medication, 80% of those with angina showing a satisfactory reduction in the number of attacks, whereas only 4% of the control group were improved. In 30 patients the effect of peritrate was compared with those of aminophylline, khellin, and theobromine calcium salicylate. The frequency of attacks during treatment with these drugs was about the same as when a placebo was given, but was reduced to one-quarter with peritrate. Exercise tolerance in angina pectoris was improved by 50% by peritrate, the effect beginning 1½ hours after administration and continuing for about 5 hours.

C. W. C. Bain